

	10	20	30	40
hGH	F P T I P	- - - - -	- - - - -	- - - - -
hPL	V Q T V P	- - - - -	- - - - -	- - - - -
pGH	F P A M P	- - - - -	- - - - -	- - - - -
hPRL	L P I C P G	G A R C Q V T	L R D L F	D R A V V L S H Y I H N L S S E M F S E
	50	60	70	80
hGH	S F L Q N P Q T S	C F S E S I P T P S N	R E E T Q Q K S N L E L L R I S L L I Q S W L E P V Q F L	D T Y Q E F E E A Y I P K E Q K Y
hPL	S F L H D S Q T S	C F S D S I P T P S N	M E E T Q Q K S N L E L L R I S L L I E S S W L E P V R F L	I D T Y Q E F E E T Y I P K D O K Y
pGH	S - T Q N A Q A A F	C F S E T I P A P T G K D E A Q Q R S D V E L L R F S L L I Q S W L G P V Q F L	A D T Y K E F E R A Y I P E G Q R Y	
hPRL	- F I T K A - I N S	C H T S S L A T P E D K E Q A Q Q N Q K D F L S L I V S I L R S W N E P L Y H L	D K R Y T - H G R G -	
	90	100	110	120
hGH	- R S V F A N S L V Y G A S D S N V Y D L L K D L E E G I O T L M G R L E D G S P R T G O I F K Q I Y			
hPL	- R S N F A N N L V Y D T S D S D Y H L L K D L E E G I O T L M G R L E D G S R R T G O I L K Q I Y			
pGH	- S R V F T N S L V Y F G T S D - R V Y E K L K D L E E G I O A L M R E L L E D G S P R A G O I L K Q I Y			
hPRL	V T E V R G M O E A P E A I L S K A V E I E O T K R L L E G M E L I V S Q V H P E T K E N E I Y P V			
	130	140	150	160
hGH	- - - - -	- - - - -	- - - - -	- - - - -
hPL	- - - - -	- - - - -	- - - - -	- - - - -
pGH	- - - - -	- - - - -	- - - - -	- - - - -
hPRL	W S G L P S L Q M A D E E S R L S A Y Y N L L H C G L R R D S H K I D N Y L K L L K C R I I H N N N C			
	170	180	190	200
hGH	S K F D T N S H N D D A L L K N - - - - -	Y G L L Y C F R K D M D K V E I F L R I V Q C R S - V E G S C G F		
hPL	S K F D T N S H N H D A L L K N - - - - -	Y G L L Y C F R K D M D K V E I F L R M V Q C R S - V E G S C G F		
pGH	D K F D T N L R S D D A L L K N - - - - -	Y G L L S C F K K D L H K A E I Y L R V M K C R R F V E S S C A E		
hPRL				

FIG.—2

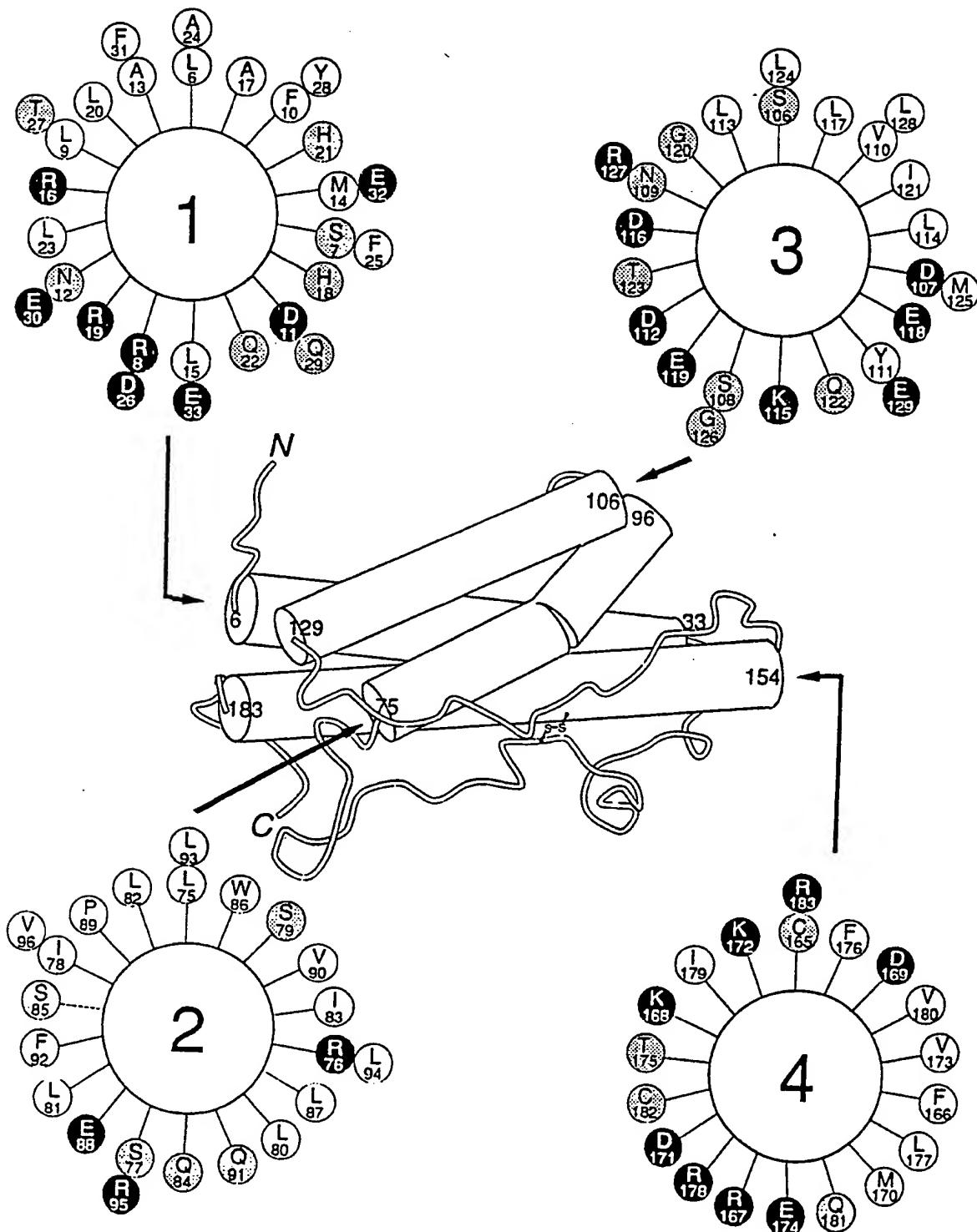


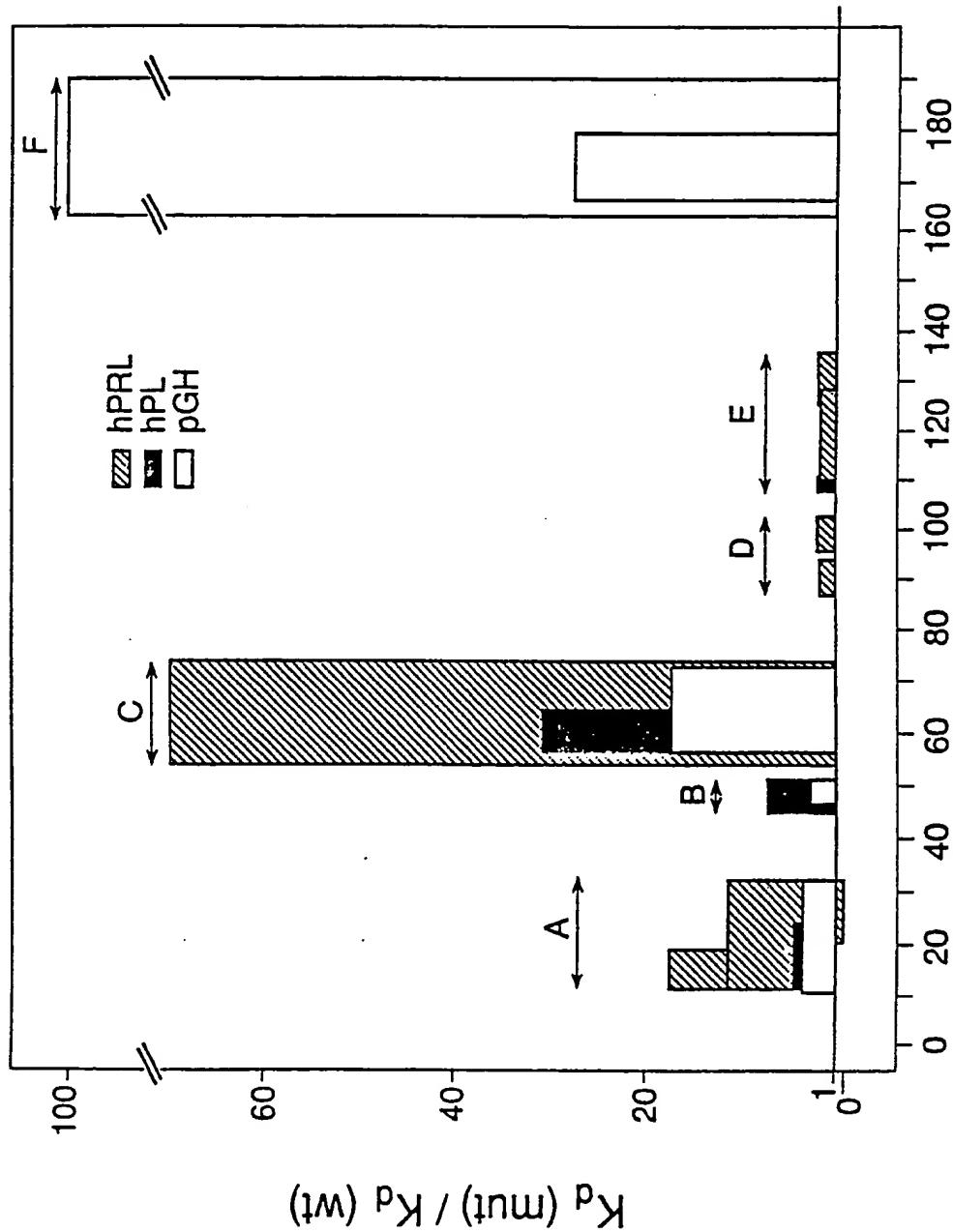
FIG.—3

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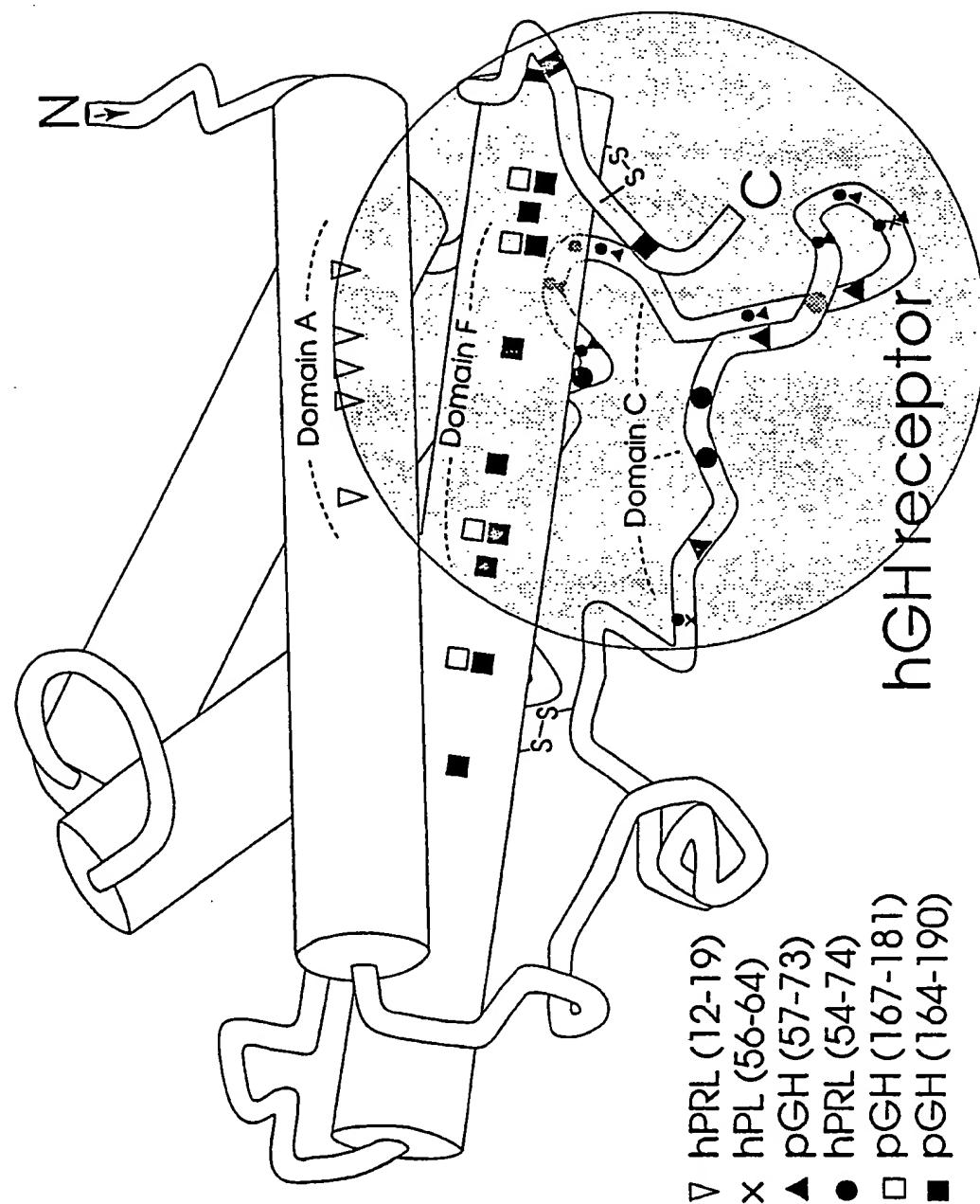
FIG.—4

Residue number in hGH



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FIG.—5



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- hPRL (88-95)
- ▲ hPRL (97-104)
- hPL (109-112)
- ✗ hPRL (111-129) minus hPRL (126-136)

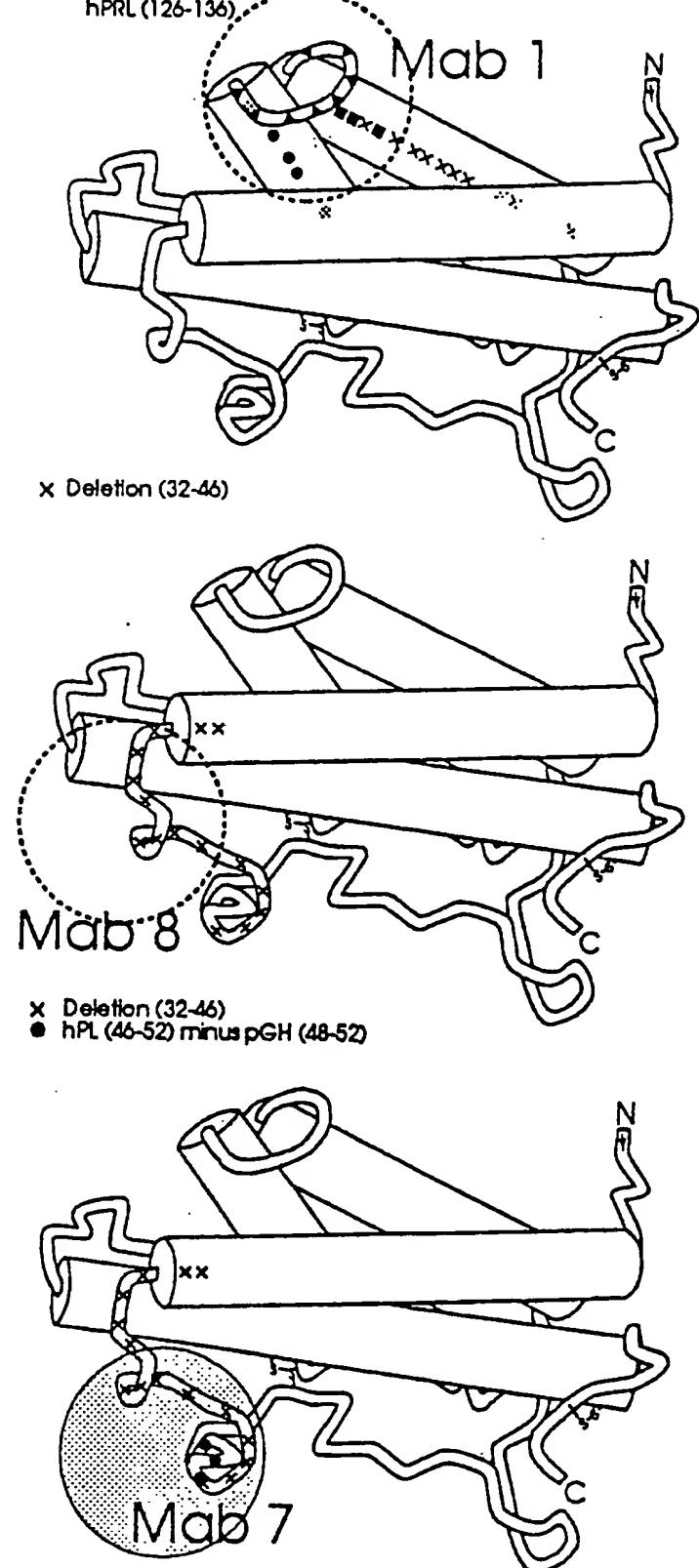
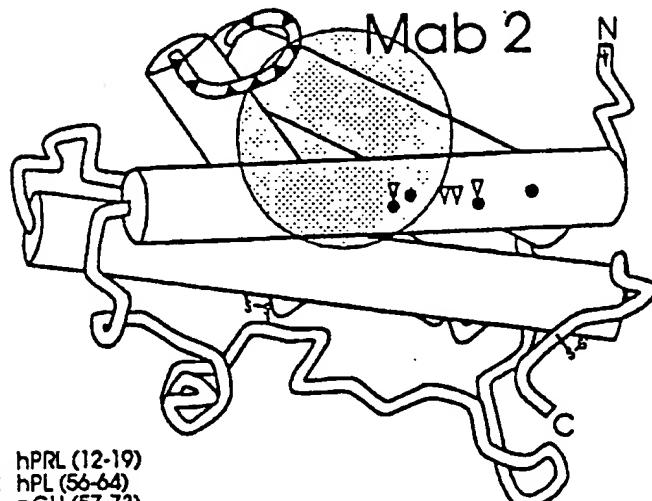


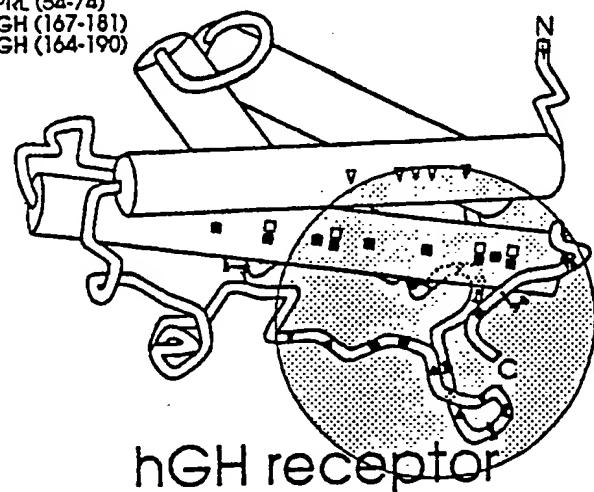
FIG.-6A

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- pGH (11-33) minus hPRL (22-33)
- ▽ hPRL (12-19) minus hPL (12-25)
- ▲ hPRL (97-104)



- ▽ hPRL (12-19)
- × hPL (56-64)
- ▲ pGH (57-73)
- hPRL (54-74)
- pGH (167-181)
- pGH (164-190)



- ▲ pGH (57-73) minus hPRL (54-74)
- pGH (164-190) minus pGH (167-181)

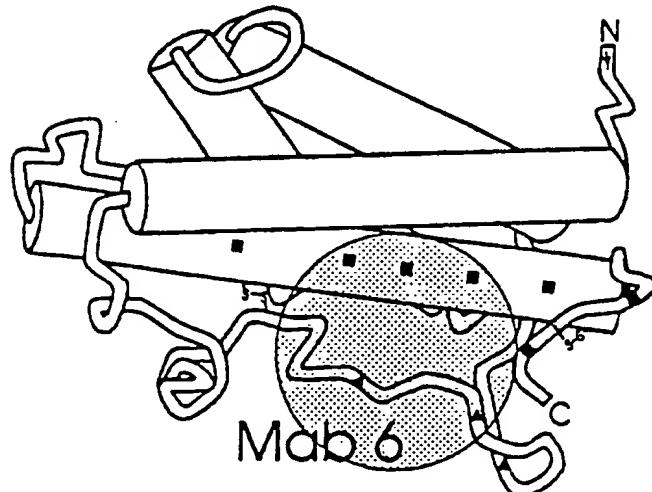
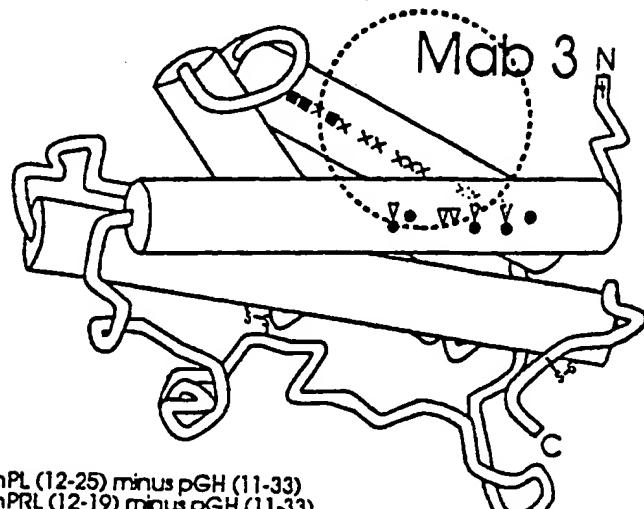


FIG.-6B

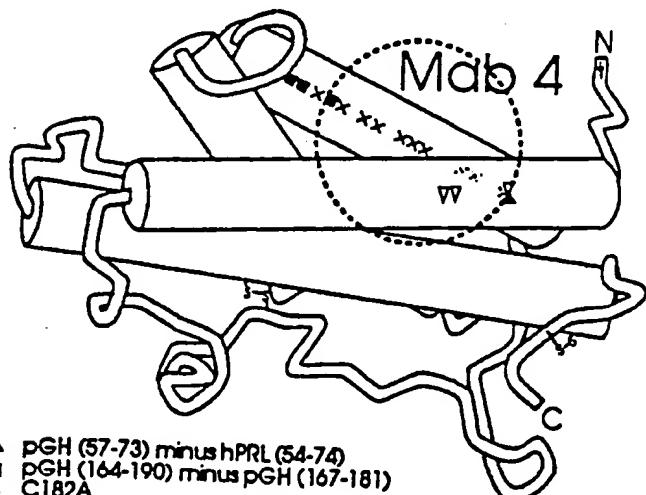
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- pGH (11-33) minus hPRL (22-33)
- ▲ hPL (12-25) minus hPRL (22-33)
- ▽ hPRL (12-79)
- hPL (109-112)
- × hPRL (111-129) minus hPRL (126-136)



- ▲ hPL (12-25) minus pGH (11-33)
- ▽ hPRL (12-19) minus pGH (11-33)
- hPL (109-112)
- × hPRL (111-129) minus hPRL (126-136)



- ▲ pGH (57-73) minus hPRL (54-74)
- pGH (164-190) minus pGH (167-181)
- C182A

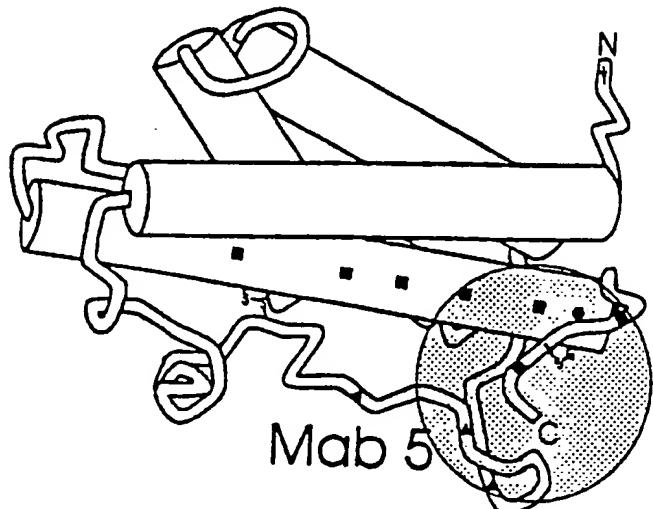
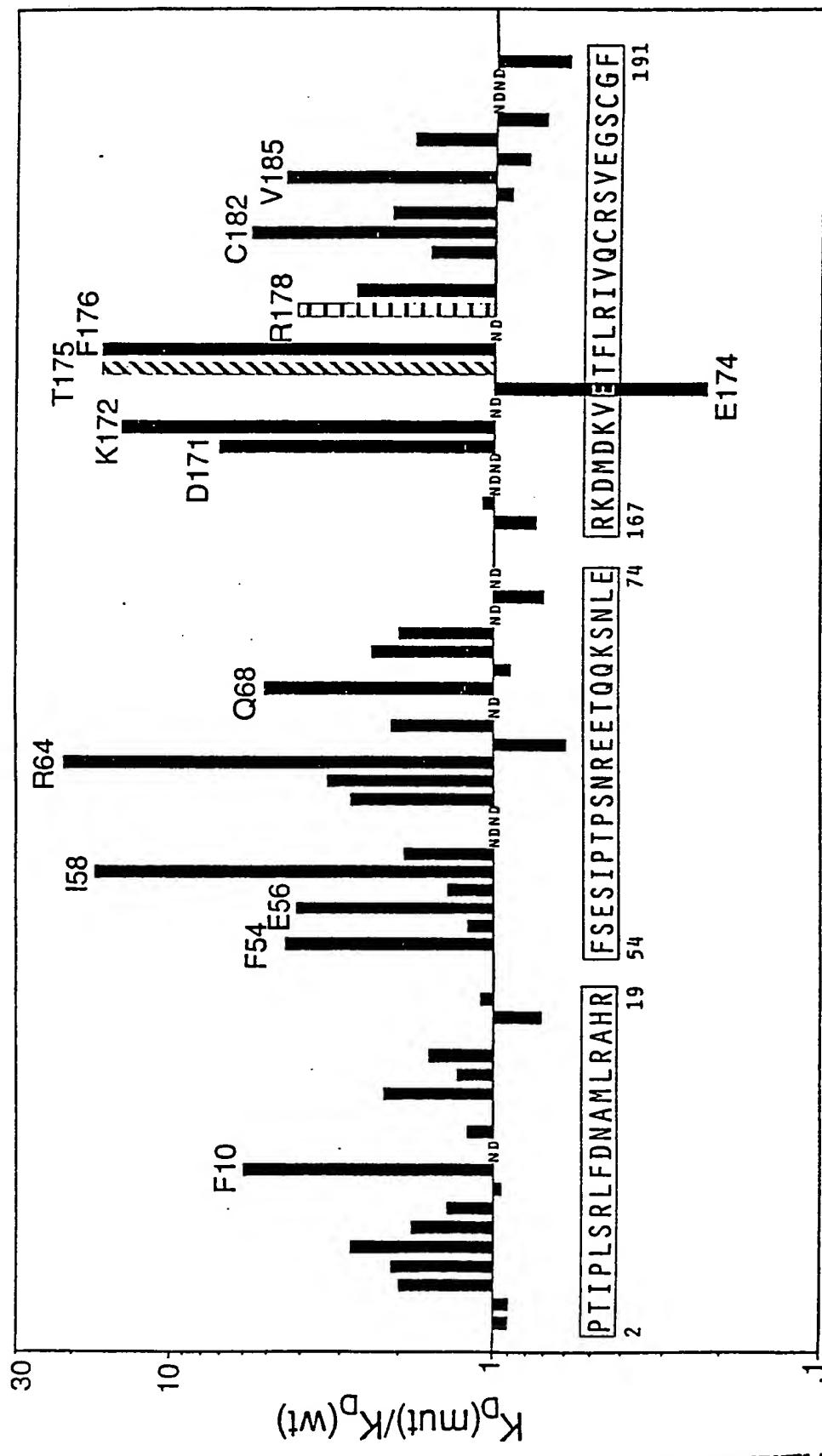


FIG.-6C

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Stronger binding → ← Weaker binding



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FIG.—7

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hGH Synthetic Gene

1 Met Lys Lys Asn Ile Ala Phe Leu Leu Ala Ser Met Phe Val Phe Ser Ile Ala Thr Asn Ala Tyr Ala
 ATG AAA AAG AAT ATC GCA TTT CTT CTC GCA TCT ATG TTC GTT TTT TCT ATT GCT ACA AAT GCC TAT GCA
 NsiI

+1 Phe Pro Thr Ile Pro Leu Ser Arg Leu Phe ASP Asn Ala Met Leu Arg Ala His Arg Leu His Gln Leu Ala
 10 79 TTC CCA ACT ATA CCA CTA AGT CGA CTA TTC GAT AAC GCT ATG CTR CGG GCC CAT CGT CTR CAT CAG CTA GCC
 NheI

Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro
 142 TTT GAC ACC TAC CAG GAG TTT GAA GAG GAA CAG TAT ATC CCC AAG GAA ACA CAA CAG AAA TCC AAC CCC
 SstI

Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys Ser Asn
 214 CAG ACC TCC CTC TGT TTC TCA GAA TCG ATT CCG ACA CCC TCC AAT CGC GAG GAA ACA CAA CAG AAA TCC AAC
 ClaI

Leu Glu Leu Leu Arg Ile Ser Leu Leu Ile Gln Ser Trp Leu Glu Pro Val Gln Phe Leu Arg Ser Val
 286 CTA GAG CTC CTC CGC ATA AGC TAC TCG CTC ATC CAG TCG TCG TCG TCG CCC GTG CAG TGC AGT GTC
 SacI

Phe Ala Asn Ser Leu Val Tyr Gly Ala Ser ASP Ser Asn Val Tyr ASP Leu Leu Lys Asp Leu Glu Glu Gly
 358 TTC GCC AAC AGC CTC GTC TAC GGC GCC TCT GAT TCG AAC GTG TAC GAC CTG AAG GAC CTA GAG GAA GGG
 NarI

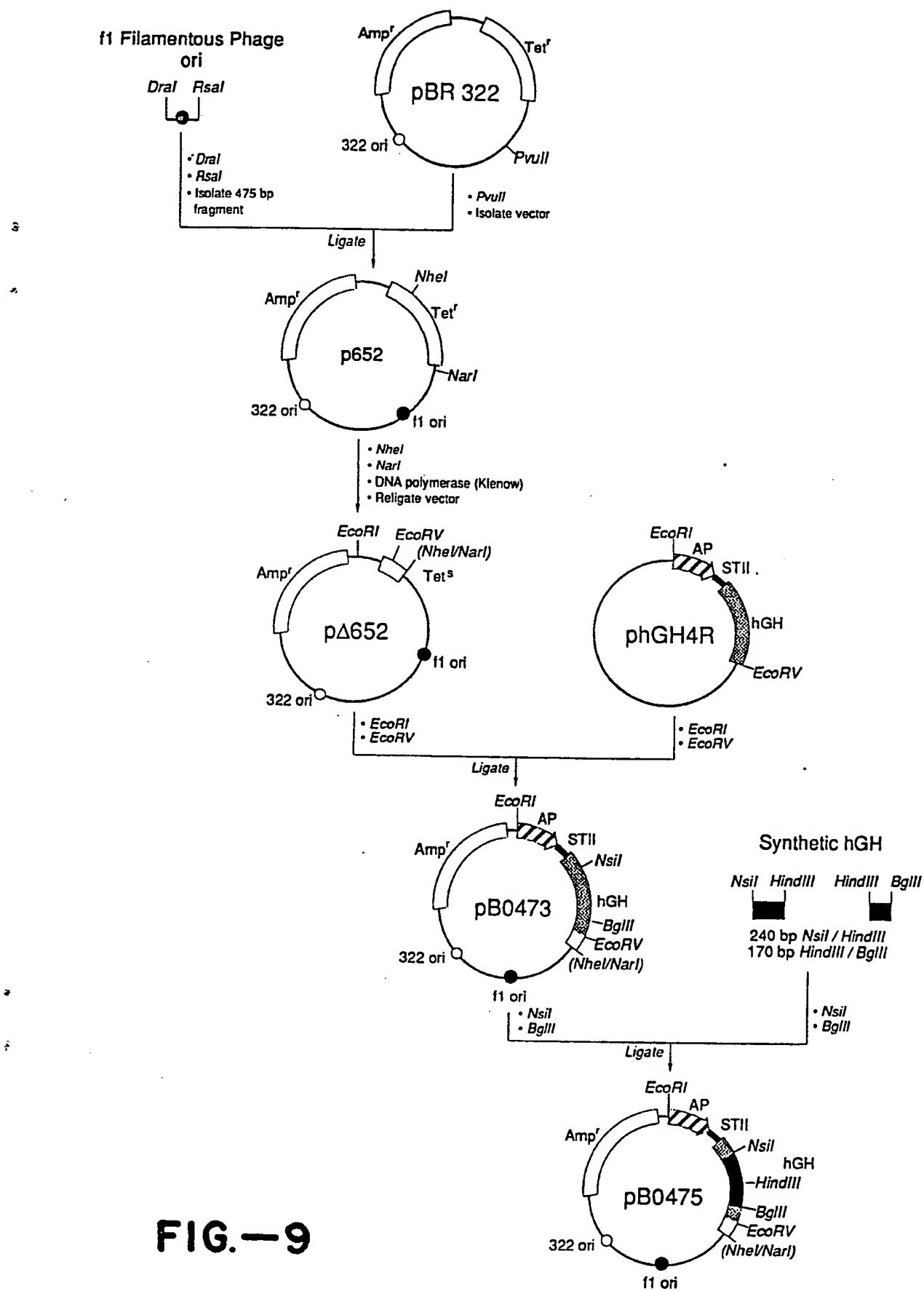
Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser
 430 ATC CAA ACG CTC ATG GGG AGG CTC GAA GAT GGC AGC CCG ACT GGG CAG ATC TTC AAG CAG ACC TAC AGC
 BglII

Lys Phe Asp Thr Asn Ser His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe Arg Lys
 502 AAG TTC GAC ACA AAC TCA CAC AAC GAT GAC GCA CTC AAC AAC TAC GGC CTC TAC GGG CTC TAC TGC TTC AGG AGC
 BglII

Asp Met ASP Lys Val Glu Thr Phe Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe AM*
 574 GAC ATG GAC AAG GTC GAG ACA TTC CGC TCT GTG CAG TGC CGC TGC CGC TCT GTG GAG GGC AGC TGT GGC TTC TAG
 PvuII

FIG.-8

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1441 *haeIII* *haeI* *scrFI*
scrFI [dcm-] *ncI*
ecori *cauII*
bstNI *sau96I* [dcm-] *nlaIII*
avarI [dcm-] *hinPI* *hgiAI*
asuI *eaI* *hhaI* *sau3AI*
ppMI *cfri* *mboI* [dam-] *asuI* *mspI*
nlary *balI* [dcm-] *mstI* *ppMI* *hpaiI*
bbVI *bstUI* *sfaNI* *aval* *fnu4HI* *eco0109I* [dcm-] *eco0109I*
ACGGAGCCGC *ACGGGGCGCA* *TCTCGGGCAG* *CCTGGTCC* *TGGCCACGGG* *TGGCATGAT* *CCTGGTCTG* *TCGTGAGGA* *CCGGCTAGG* *CTGGGGGT*
GTCGTGGG *TGGCCGGT* *AGACCCGGG* *ACCGGTGCC* *ACCAACCCAGG* *GCACGAGAC* *AGCAACTCC* *GGCCGATCC* *GACCGCCCA*

1541 *thaI* *fnu4HI*
fnu4HI *thaI* *fnu4HI* *mbolI*
fnu4HI *fnu4HI* *aval* *fnu4HI* *mbolI*
bstUI *sfaNI* *aval* *fnu4HI* *mbolI* [dam-] *mbolI*
bbVI *bbVI* *bbVI* *bbVI* *bbVI*
bsrI *hphI* *hphI* *hphI* *hphI* *hphI*
CGCTTACG *CGTAGGAGA* *TGAATACCG* *ATACGGAGC* *GAACGTGAAG* *CGACTGCTGC* *TGCCAAACGT* *CTGGGACCTG* *AGCAACACA* *TGAATGGTCT*
ACGGATGAC *CATCGCTT* *ACTTAGGGC* *TATGGCTCG* *CTTGGCACTC* *GCTGACGACG* *ACGTGACG* *GACCTGGAC* *TGCTGTGTGT* *ACTTACCGA*

1641 *thaI* *fnu4HI*
fnu4HI *thaI* *hhaI* *hhaI* *hhaI* *hhaI* *hhaI*
bstUI *bstUI* *bstUI* *bstUI* *bstUI* *bstUI*
CGGGAAAGTC *AGCGCCCTGC* *ACCATTTATGT* *TCCGGATCTG* *CATGGCAGGA* *TGCTGCTGGC* *TACCCCTGTGG*
ACGGCAAGGC *ACAAAGCAT* *TCAGACCTTT* *GGCCTTCAG* *TCGGGGGACG* *TGGTAATACA* *AGGCCTAGAC* *GTAGGGTCTT* *ACGACGACCC* *ATGGGACACC*

1741 *hinPI* *hinPI* *hinPI* *hinPI* *hinPI*
haeII *haeII* *haeII* *haeII* *haeII*
mseI *ddeI* *ddeI* *ddeI* *ddeI*
CGAACGGCTG *CGATTGACCC* *TGAGTGATTT* *TTCCTGGTC* *CCGGCGATTC* *CATAACCGCA* *GTTGTTTAC* *CTCACAACTG*
TGTGGATGT *AGACATAATT* *GCTTCGCGAC* *CGTAACTGGG* *ACTCACTAA* *AAGAGACAG* *GGCCGGTAG* *GTATGGGGT* *CAACAAATGG* *GAGTGTGCA*

scrFI
ncI *foKI*
mspI *mspI* *foKI*
nsPcIX *nsPcIX* *foKI*
hpaiI *hpaiI* *foKI*
cauII *nlaIII* *nlaIII* *foKI*
TCCAGTAACC *GGGCATGTTTC* *ATCATCAGTA* *ACCCGTTATCG* *TGAGGATCCCT* *CTCTCGTTTC* *ATCGGTTATCA* *TTACCCCCAT* *GAACAGAAAT* *TCCCCCTTAC*
AGGTCAATTG *CCCGTACAAG* *TAGTAGTCAT* *TGGCATAGC* *ACTCGTAGGA* *GAGGCAAG* *TAGCCATAGT* *ATGGGGGTA* *CTTGTCTTA* *ACGGGGAAATG*

FIG.-10D

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1941	ACGGAGGCAT TGCTCTCGTA	CAAGTGACCA GTTCACTGGT	AACAGGAAAA TTGTCCTTT	AACCGCCCTT TTGACCGGGAA	GCTTATTCAG CGAAATAGTC	AAGCCAGACA ACCTCTGTA	TAAACCGCTTC AACCTAGTC	TGGAGAAACT TTCTGGTGT	CAACGAGCTG ACCTCGAAG	alui alui
2041	lgaI GACGGGATG CTGGCCTAC	foki AACAGGGAGA TGTGCCGCT	TCGCTTCACG AGCGAAGTGC	ACCACCGCTGA GTAGACACTT	TTAGCTGAA AGCGAAGTGC	AAATCAGCTC TGGTGGACT	ATTTCAGCTC ACTCGAAATG	TGAGCTTAC TTAGGAAATA	AAATCAGCTA AACGTTAAATA	alui alui
2141	thaI fnudII bstU	xmnI bstU	hinFI	alui	mseI	haeIII AAATCAGCTC TTAGCTGAG	AAATCAGCTC GTATCCCG	AAATCAGCTA TTAGGAAATA	AAATCAGCTA AACGTTAAATA	mseI mseI
2241	lgiI bsrI	thaI fnudII bstU	hinFI	alui	mseI	haeIII AAATCAGCTC TTAGCTGAG	AAATCAGCTC GTATCCCG	AAATCAGCTA TTAGGAAATA	AAATCAGCTA AACGTTAAATA	haeIII mseI
2341	phI	mspI mspI	mspI	alui	mspI	mspI alui	mspI alui	mspI alui	mspI alui	mspI alui

FIG. 1—OE

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2441	GGCGAACGTG CGCCTGGAC	mboI I mboI I	hinPI hhaI haeII bbVI	hinPI hhaI haeII bbVI	thaI fnuDII bstUI [M. hhaI-] hinPI hhaI fnu4HI	thaI fnuDII bstUI [M. hhaI-] hinPI hhaI fnu4HI
2541	CCGGCTTAATG CCGGAAATAC	GGCCGGCTACA GGGGCGATGT	GGATCCGCC CCCCGGACGG	GGGGCATGAC CCTAGGACGG	GGGTGATGAC GCCACIACTG	GGGTGAAAAC CCACTTTGG
2641	CAGCTTGCT GTCGAAACAGA	GTAAAGGGAT CATTCGGCTA	GCGGGAGCA CGGGCCCTGT	GACAAGCCG CTGTCGGGC	TCAAGGGGTG AGTCCCCGGC	TGGGGGGTG AGTCGCCCCAC
2741	CGATACCGGA GCTATCGCT	accI GCTTAACTG CACATATGAC	mseI GCTTAACTAT CGAATTGATA	sfanI fnu4HI GGGGCATCAG CGCCGTAGTC	rsal apal ndel bstUI [M. hhaI-] hinPI hhaI fnu4HI	rsal apal ndel bstUI [M. hhaI-] hinPI hhaI fnu4HI
2841	AAAAATACCG CTTTATCGG	sfaNI sfaNI	earI hinPI hhaI	sfanI fnu4HI GGGGCATCAG CGCCGTAGTC	ddel bstI 1286 rsal apal ndel bstUI [M. hhaI-] hinPI hhaI fnu4HI	sfanI fnu4HI GGGGCATCAG CGCCGTAGTC

FIG. - 10F

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FIGURE 10

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FIG. 101

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bglI (GCCNNNNNGCC) :	3989 [M. haelli-]
bglII (AGATCT) :	867
bsmI (GAATCC) :	182 455 1390
bsmII (CTTCCTC) :	295 977 2631 3942 4707
bsp1286 (GCGGHC) :	504 [M. haelli-] 677 [M. aluI-]
bsp1287 (TCAGA) :	3702 4710 4815
bsp1288 (ACCTGC) :	792
bsp1289 (TCCGGA) :	1701 2108 2568
bsp1290 (ACTGG) :	706 860 1220 1547
bsp1291 (TTCGAA) :	1818 1842 2250 2729 2757 3385 3398 3515 3921 4039 4082 4346
bsp1292 :	4521
bsp1293 (TTCGAA) :	778
bsp1294 (CCMGG) :	541 757 1140 1479 3009 3130 3143
bsp1295 (CCGGG) :	211 [M. hhaI-] 647 855 1271 1281 1426 1452 1574 1671 2043 2144 2520 [M. hhaI-] 2540 [M. hhaI-]
bsp1296 (CCANNNNTGG) :	2564 [M. hhaI-] 2582 [M. hhaI-] 2584 [M. hhaI-] 2687 [M. hhaI-] 3028 3609 [M. hhaI-] 3939
bsp1297 (RGATCY) :	4432 [M. hhaI-] 4764 [M. hhaI-]
bsp1298 (CCTNAGG) :	750
bsp1299 (CCSGG) :	816 867 1704 2105 2571 3623 3634 3720 3732 4500 4517
bsp1300 (YGGCC) :	733
bsp1301 (ATCGAT) :	1180 1295 1521 1849 2627 2662 3361 4057 4408
bsp1302 (ATCGAT) :	290 1481 4263
bsp1303 (CTNAG) :	625
bsp1304 (CTNAG) :	573 619 734 1618 1780 2792 3257 3666 3832 4372 4798
bsp1305 (GATC) :	139 817 868 1498 1705 2106 2572 3549 3624 3635 3643 3721 3733 3838 4179 4197
bsp1306 (TTTAA) :	4243 4501 4518 4554
bsp1307 (CAGNNNGTG) :	3739 3758 4450
bsp1308 (GATC) :	2332
bsp1309 (GGCCG) :	574 619 734 1618 1780 2792 3257 3666 3832 4372 4798
bsp1310 (GGCCG) :	290 1481 4263
bsp1311 (CTCTTC) :	290
bsp1312 (CCTNAGG) :	551 2860 4664
bsp1313 (CCNNNNNAGG) :	733
bsp1314 (CTNNNNNAGG) :	793
bsp1315 (RGGNCCY) :	801 1475 [dcm-] 1517 4850
bsp1316 (GAATTG) :	1
bsp1317 (CCWGG) :	541 757 1140 1479 3009 3130 3143
bsp1318 (GATATC) :	1195
bsp1319 (GCGGC) :	204 207 697 849 940 1002 1017 1033 1236 1245 1324 1443 1453 1467 1596 1599
bsp1320 (GCGGC) :	1722 1803 2516 2538 2621 2718 2771 2887 2905 2908 3026 3181 3324 3389 3392
bsp1321 (CGGG) :	3598 3926 4115 4265 4292 4387 4616
bsp1322 (GGATG) :	211 647 855 1271 1281 1426 1452 1574 1671 2043 2144 2520 2540 2564 2582 2584
bsp1323 (GGATG) :	238 703 1122 1143 1718 1807 1885 2046 2657 3855 4036 4323
bsp1324 (TGGGCA) :	987 1393 1491 4095
bsp1325 (WGGCCW) :	555 1481 2995 3006 3458
bsp1326 (RGCGCY) :	153 767 1242 1681 1764 2484 2492 2856 3226
bsp1327 (GGCC) :	291 505 556 1183 1298 1482 1986 2186 2328 2996 3007 3025 3459 3917 3997 4264
bsp1328 :	4851

FIG.—10K

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hyal (GACGCC) : 917 1277 1427 2041 2565 2688 3084 3662 4412
 hyal (GAGCWC) : 677 [M. aluI-] 1502 2798 3296 4457 4542
 ligI (GGYRCC) : 767 1086 1129 1326 2374 3823
 heII (GRGCCY) : 504 677 719 2408
 hial (GGCC) : 112 154 210 768 988 1111 1243 1394 1456 1492 1682 1765 2485 2493 2519 2541 2550
 hanPI (GGCC) : 2563 2583 2686 2716 2857 2890 3160 3227 3327 3501 3610 4003 4096 4433 4765
 hanII (GTYRAC) : 112 154 210 768 988 1111 1243 1394 1456 1492 1682 1765 2485 2493 2519 2541 2550
 hindII (GRYRAC) : 2563 2583 2686 2716 2857 2890 3160 3227 3327 3501 3610 4003 4096 4433 4765
 hindIII (AAGCTT) : 477 4414
 hinfI (GGATC) : 71 691
 hincII (CCGG) : 623 [M. tagI-] 628 [M. tagI-] 776 [M. tagI-] 1341 [M. tagI-] 1562 [M. hphI-] 2068 2264
 hphI (GGTGA) : 1171 1180 1295 1321 1522 1702 1849 2109 2439 2569 2628 2662 3189 3336 3362 3552
 hincII (GAGGA) : 3956 3990 4057 4167 4409
 hincII (GATC) : 380 1136 1344 1565 2346 2592 2601 3726 3953 4349 4575 4590
 hincII [dam-] (GATC) : 409 514 551 744 842 870 [dam-] 1638 2465 2861 3632 [dam-] 3723 [dam-] 4478 4556 [dam-]
 hincII (CCTC) : 4665 4861
 hincII (TTAA) : 139 817 868 1498 1705 2106 2572 3549 3624 3635 3643 3721 3733 3838 4179 4197
 hincII (CCTNAGG) : 4243 4501 4518 4554
 hincII (CCTNAGG) : 148 163 241 372 378 554 606 610 639 650 682 736 771 809 835 1013 1125 1185 1265
 hincII (CCGGCC) : 1303 1330 1516 1830 1888 1944 2372 2579 2609 2871 3097 3154 3421 3821 3902 4032
 hincII (CCGGCC) : 4238 4849
 hincII (TTAA) : 69 257 324 1044 1066 1757 1979 2011 2125 2136 2148 2159 2176 2274 2545 2763
 hincII (CCGG) : 3688 3740 3745 3759 3812 4047 4086 4451 4823
 hincII (CCATG) : 1171 1180 1295 1321 1522 1702 1849 2109 [M. bamHI-] 2439 2569 [M. bamHI-] 2628 2662
 hincII (TGCCCA) : 987 1393 1491 4095
 hincII (CCTNAGG) : 733
 hincII (GGGGCC) : 1320 2438
 hincII (GGGGCC) : 767
 hincII (CCSGGG) : 1180 1295 1521 1849 2627 2662 3361 4057 4408
 hincII (CATATG) : 2804
 hincII (GCTAGC) : 523 [M. aluI-] 1239
 hincII (CATG) : 40 964 1288 1495 1629 1854 1918 1983 2618 2723 2983 3703 4194 4204 4282 4318
 hincIV (GGNNCC) : 4711 4816
 hincII (TCCGCA) : 504 767 816 1086 1129 1291 1326 1361 1475 1518 1797 2105 2374 2395 2407 2571
 hincII (ATGCA) : 3012 3051 3823 3917 3958 4169 4759
 hincII (ATGCAT) : 646
 hincII (ATGCAT) : 453
 hincII (ATGCAT) : 1853 2617 2982
 hincII (ATGCAT) : 716
 hincII (ATGCAT) : 14 1352 1401
 hincII (ATGCAT) : 2264 2286 2882 3353 3870
 hincII (ATGCAT) : 801 1475 1517
 hincII (ATGCAT) : 590 4116 [M. HI-]

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PvuI(CGATCG):
 PvuII(CAGCTG): 4242
 RsaI(GTAC): 270 1018[M.H1-]
 SacI(GGCTC): 159 342 787 1174 2789 4354
 SalI(GTCGAC): 677
 Sau3AI(GATC): 854
 SmaI(GGCCG): 477
 SmaI(GGCCG): 139 817 868 1498 1705 2106 2572 3549 3635 3643 3721 3733 3838 4179 4197
 SmaI(GGCCG): 4243 4501 4518 4554
 SmaI(GGCCG): 504 [M.haeIII-] 505 [M.haeIII-] 1297 [M.haeIII-] 1476 [dcm-]
 SmaI(GGCCG): 1518 1797 1986 [M.haeIII-] 2328 [M.haeIII-] 3917 [M.haeIII-] 3996 [M.haeIII-] 4013
 SmaI(AGTACT): 4235 4851 [M.haeIII-]
 SmaI(CCSCGG): 4353
 SmaI(CCSCGG): 1180 1295 1521 1849 2627 2662 3361 4057 4408
 SmaI(CCSCGG): 541 757 1140 1479 3009 3130 3143
 SmaI(GCATC): 175 237 416 930 1144 1214 1458 1710 1719 1806 1884 1947 2658 2774 2829 2850
 SmaI(TACGTA): 3070 4122 4332 4562
 SmaI(ACTACT): 217
 SmaI(AATT): 338
 SmaI(GAGCTC): 2127 4677
 SmaI(GAGCTC): 677
 SmaI(AGCCCT): 555
 SmaI(CCCTGG): 567 1406
 SmaI(TCGA): 478 486 626 [M.claI-] 717 779 894 975 1305 2370 3082 4526
 SmaI(TCGA): 211 647 855 1271 1281 1426 1452 1574 1671 2043 2144 2520 2564 2582 2584
 SmaI(TCGC): 2687 3028 3609 3939 4432 4764
 SmaI(TCGC): 968 2726
 SmaI(TCTAGA): 368
 SmaI(TCTAGA): 716
 SmaI(TCTAGA): 816 867 1704 2105 2571 3623 3634 3720 3732 4500 4517
 SmaI(TCTAGA): 290
 SmaI(TCTAGA): 623 2068 4470
 SmaI(TCTAGA): not found
 SmaI(TCTAGA): KpnI(GGTACC), asp718(GGTACC), avrII(CCTAGG), bssHII(GGCCG), bstEII(GGTNACC), esPI(GCTNAGC), hpaI(GTTAAC), kpnI(GGTACC), mluI(AGCGGT), ncoI(CCATGG), notI(GGGCCGC), rsrII(CGGWCGC), smaI(GCCGGC), sphiI(GCATGC), xmaI(CCCGGG)

FIG.—10M

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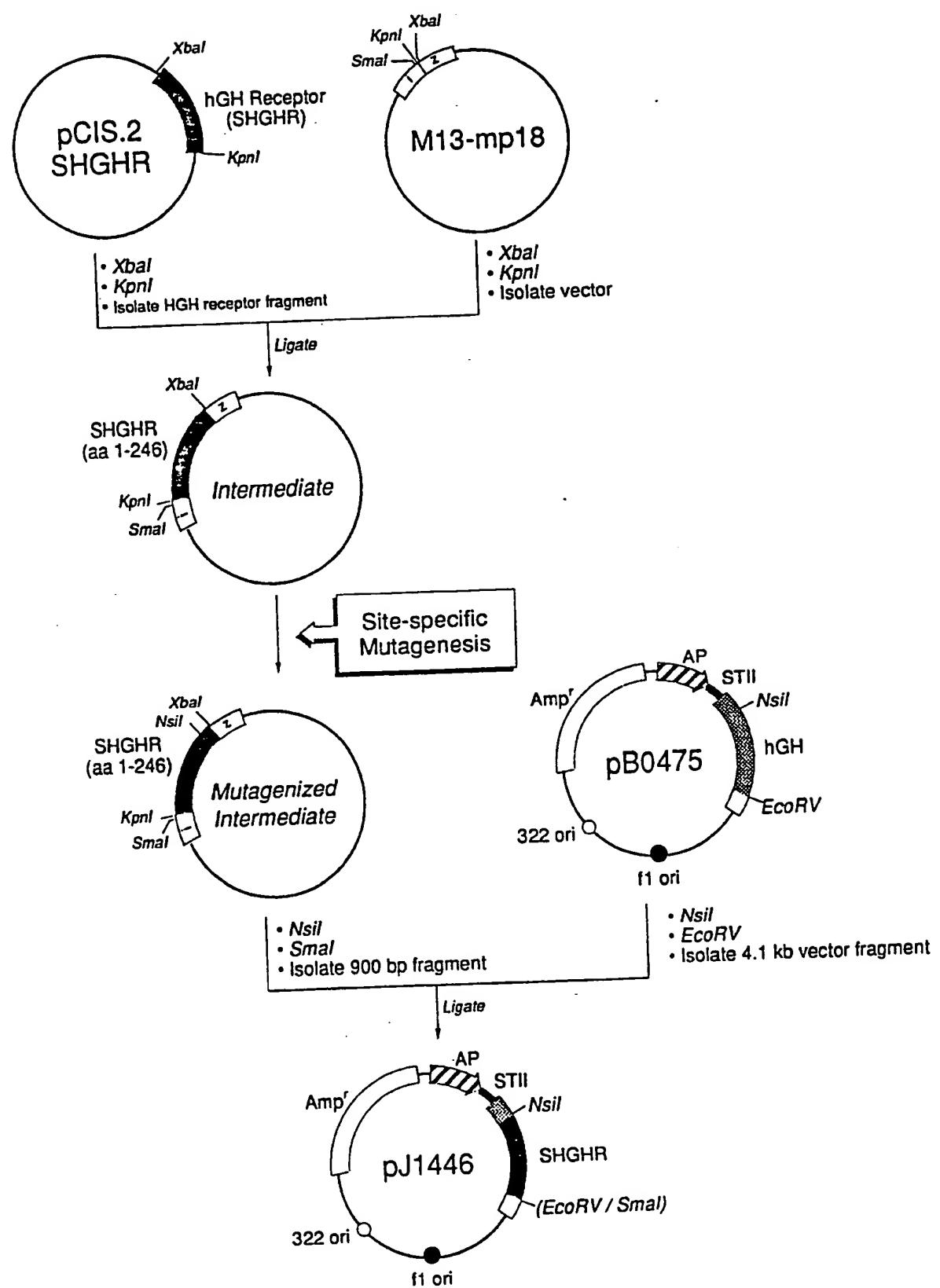


FIG.-II

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FIG-128

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FIG. 12C

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FIG.—12D

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W
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I
G.
F

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FIG.—12G

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4001	TICATCCATA GTGCCCTGAC TCCCCGGTACGT GTAGATAACT ACGATACGGG AGGGCTTACG ATCTGGCCC TCCCGAATGG TAGACCGGGG TCACGACGTT	bsRI hinfI fokI mspI hpaII hpaII cauII aluI GTTGGGGGA AGCTTAGAGTA AGTAGTTCGC CAGTTAAATAG TTTGCGCAAC GTGCTGGTGC AAACGCGTTG CAAACAACGGT	sau96I [M. haeIII-] nlaIV haeIII asuI bglI [M. haeIII-] hpaII mspI hpaII hpaII cauII aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	bsmaI thaI fnu4HI bbvI bglI [M. haeIII-] hpaII mspI hpaII hpaII cauII aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC
4101	AGTAGTTAGTCAAC GGGCCGGACT CAATAGTGTAC TCTTCATTCA	mspI hpaII hpaII cauII aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	sau96I [M. haeIII-] nlaIV haeIII asuI bglI [M. haeIII-] hpaII mspI hpaII hpaII cauII aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	bsRI fokI mspI hpaII hpaII cauII asuI bglI [M. haeIII-] hpaII mspI hpaII hpaII cauII aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC
4201	AGCTCCGGTA AGCTGGTGTG CCAACCGATC AAGGCAGATT ACATGATCCC CCATGTTGGTGC CAAAAAAGCG GTTAGCTCCT AACGACGTTG CAAACAACGGT	scrFI ncII mspI hpaII cauII aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	haeIII sau3AI nlaIV aluI nlaIV aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	bsRI fokI mspI hpaII hpaII cauII asuI bglI [M. haeIII-] hpaII mspI hpaII hpaII cauII aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC
4301	GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC CATCGCTAAG ATGCTTTCT GTGACTGGTG	scrFI mspI hpaII cauII aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	sau3AI mboI [dam-] dpnI alwI nlaIV dpnI alwI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	bsRI fokI mspI hpaII hpaII cauII asuI bglI [M. haeIII-] hpaII mspI hpaII hpaII cauII alwI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC
4401	AGAAGTAAGT TGGCCGGACT CAATAGTGTAC TCTTCATTCA	scrFI mspI hpaII cauII aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	fnu4HI haeIII eaeI cfrI nlaIV aluI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	bsRI fokI mspI hpaII hpaII cauII asuI bglI [M. haeIII-] hpaII mspI hpaII hpaII cauII alwI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC
4501	AGTACTCAAC CAAGTCATTG TGAGAATAGT GTATGGGGGC ACCGAGTTGCACTTC TGGCTCAACG GGATATAACCG CCTTCATCCGG CCTCAACACGG CCTGGGTGTC CCTATTATGG GCAGGAACTTC CCTCTCTCAA	scrFI mspI hpaII cauII alwI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	hinfI hpaII fnu4HI bbvI nlaIV alwI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC	bsRI fokI mspI hpaII hpaII cauII asuI bglI [M. haeIII-] hpaII mspI hpaII hpaII cauII alwI GGCTTCATTG CGGAACTGGT CAATGACTTC ATGGTTATGG CAGGCACTGC TAATCTCTT ACTGTCATGC

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FIG.—12 J

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aixi (GGATC) : 851 1095 1339 1340 1852 2253 2254 2719 2720 3697 3771 3783 3868 3881 4345 4648
 aixi (GATC) : 4666
 aixi (GTCAC) : 3541
 aixi (ATTAT) : 2946 3444 4690
 asei (ATTAT) : 4194
 asei (GGNCC) : 641 1024 1445 1624 1666 1945 2134 2476 4065 4144 4161 4383 4999
 awei (CYCGRG) : 1610
 awei (GGGCC) : 641 1024 1624 [dcm-] 1666 1945 4161 4383
 awei (TGGCAT) : 453
 awei (CCATGG) : 637
 awei (TGGCCK) : 1629 [dcm-]
 bamH1 (GGATCC) : 1339 2253 [M. mspI-] 2719 [M. mspI-]
 hanI (GGYRC) : 1474 2522 3971
 hanII (GRGCYC) : 2556
 hanII (GCAGC) : 204 207 479 1221 1384 1591 1615 1744 1747 1870 2664 2769 2866 3035 3053 3472
 bclI (dam-) (TGATCA) : 3537 3540 3746 4074 4263 4440
 bclI (GCCNNNNNGGC) : 138
 bclI (GAATGC) : 182 701 1289 1538
 bclI (GTCTC) : 295 587 2779 4090 4855
 bspI 286 (GCGGHC) : 495 1139 1650 2556 2946 3444 4605 4690
 bspHI (TCATGA) : 3850 4858 4963
 bspII (TCGGGA) : 1849 2256 2716
 bsRI (ACTGG) : 603 870 896 1049 1368 1695 1966 1990 2398 2877 2905 3533 3546 3663 4069 4187
 bstNI (CCWGG) : 4230 4494 4669
 bstNI (GGCG) : 501 524 1627 3157 3278 3291
 bstNI (CGCG) : 211 [M. hhaI-] 1203 1419 1429 1574 1600 1722 1819 2191 2292 2668 [M. hhaI-] 2688 [M. hhaI-]
 bstXI (RCATCY) : 2712 [M. hhaI-] 2730 [M. hhaI-] 2732 [M. hhaI-] 2835 [M. hhaI-] 3176 3757 [M. hhaI-] 4087
 bstXI (RCATCY) : 4580 [M. hhaI-] 4912 [M. hhaI-]
 caII (CCSGG) : 850 1094 1339 1852 2719 3771 3782 3868 3880 4648 4665
 cfrI (YGGCGR) : 1443 1669 1997 2775 2810 3509 4205 4556
 cleI (CTNAG) : 290 1199 1629 4411
 clpNI (GATC) : 57 488 546 579 1158 1766 1928 2940 3405 3814 3980 4520 4946
 drahI (TTAAA) : 139 851 1095 1340 1646 1853 2254 2720 3697 3772 3783 3791 3869 3881 3986 4327
 drahI (CACNNNGTG) : 4345 4391 4649 4666 4702
 drahI (CACNNNGTG) : 3887 3906 4598
 eaeI (YGGCGR) : 562 2480
 eaeI (YGGCGR) : 290 1199 1629 4411
 eagi (CGGCCG) : 290 1199
 earI (CTCTTC) : 3008 4812
 eco0109I (RGGNCCY) : 640 1623 [dcm-] 1665 4998
 ecorI (GAATT) : 1
 ecorI (CCWGG) : 501 524 1627 3157 3278 3291
 ecorI (GATATC) : 911

FIG.-12K

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fnuII (GC:GGC) : 204 207 479 1198 1201 1221 1384 1393 1472 1591 1594 1601 1615 1744 1747 1870
 1951 2664 2686 2700 2769 2866 2919 3035 3053 3056 3174 3329 3472 3537 3540 3746
 4074 4263 4413 4440 4535 4764
 211 1203 1419 1429 1574 1600 1722 1819 2191 2292 2668 2712 2730 2732 2835
 3176 3757 4087 4580 4912
 fokI (GGATG) : 238 811 959 963 1866 1955 2033 2194 2805 4003 4184 4471
 fspI (TGGCA) : 1541 1639 4243
 haei (WGGCCW) : 471 526 1629 3143 3154 3606
 haeiI (RGCCCY) : 153 1390 1829 1912 2632 2640 3004 3374
 haeliI (GGCC) : 291 472 527 1200 1446 1630 2134 2334 2476 3144 3155 3173 3607 4065 4145 4412
 4999
 hqaiI (GACCC) : 1425 1575 2189 2713 2836 3232 3810 4560
 hgaiI (GGGCC) : 495 1139 1650 2946 3444 4605 4690
 hgiciI (GGYRC) : 1474 2522 3971
 hqjII (GRGCC) : 2556
 hhaiI (GGCC) : 112 154 210 1391 1542 1604 1640 1830 1913 2633 2641 2667 2689 2698 2711 2731
 2834 2864 3005 3038 3308 3375 3475 3649 3758 4151 4244 4581 4913
 112 154 210 1391 1542 1604 1640 1830 1913 2633 2641 2667 2689 2698 2711 2731
 hjnpI (GGCC) : 2834 2864 3005 3038 3308 3375 3475 3649 3758 4151 4244 4581 4913
 hincII (GTYRAC) : 1206 4562
 hindII (GTYRAC) : 1206 4562
 hinII (GGCTT) : 71
 hinfi (GAACTC) : 505 685 901 1489 [M.hphI-] 1710 [M.hphI-] 2216 2412 2434 3030 3105 3501 4018
 1206
 hpaI (GTTAAC) : 1443 1469 1670 1850 1997 2257 2587 2717 2776 2810 3337 3484 3510 3700 4104 4138
 4205 4315 4557
 hphI (GGTGA) : 380 561 575 1492 1713 2494 2740 2749 3874 4101 4497 4723 4738
 409 542 1181 1184 1786 2613 3009 3780 [dam-] 3871 [dam-] 4626 4704 [dam-] 4813
 5009
 mbolI (dam-) (GATC) : 139 851 1095 1340 1646 1853 2254 2720 3697 3772 3783 3791 3869 3881 3986 4327
 4345 4391 4649 4666 4702
 mnII (CCTC) : 148 163 241 372 378 470 614 759 865 1136 1157 1413 1451 1478 1664 1978 2036
 2092 2520 2727 2757 3019 3245 3302 3569 3969 4050 4180 4386 4997
 69 257 324 519 744 893 1207 1905 2127 2159 2273 2284 2296 2307 2324 2422 2693
 2911 3836 3888 3893 3907 3960 4195 4234 4599 4971
 1443 1469 1670 1850 1997 2257 [M.bamHI-] 2587 2717 [M.bamHI-] 2776 2810 3337 3484
 3510 3700 4104 4138 4205 4315 4557
 1541 1639 4243
 1468 2586
 1443 1669 1997 2775 2810 3509 4205 4556
 2952
 1387

FIG.—I2L

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mlaII (CATG) :
 nspCI (RCATGY) : 40 597 623 905 1176 1332 1436 1643 1777 2002 2066 2131 2766 2871 3131 3851 4342
mlaII' (GGNNCC) :
 nleI (GAGTC) : 4352 4430 4466 4859 4964
 ppumI (RGGWCCY) : 550 641 1024 1339 1439 1474 1509 1623 1666 1945 2253 2522 2543 2555 2719 3160
mrI (GGGGCCGC) :
 nslI (ATGCCAT) : 3199 3971 4065 4106 4317 4907
 nspCI (RCATGY) : 1198
mlaII (CCANNNNTGG) :
 nleI (GAGTC) : 453
 ppumI (RGGWCCY) : 1175 2001 2765 3130
mlaII (CGATCG) :
 pvlI (CAGCTG) : 14 1500 1549
mlaII (GATC) :
 sau3AI (GATC) : 505 685 2412 2434 3030 3501 4018
mlaII (RGGMCC) :
 pslI (CTGCCAG) : 640 1623 1665
mlaII (M.H1-) :
 pvlI (CGATCG) : 4264 [M.H1-]
mlaII (CAGCTG) :
 pvlI (CAGCTG) : 4390
mlaII (GATC) :
 sau3AI (GATC) : 270 650 733
mlaII (GGNCC) :
 sau96I (GGNCC) : 159 342 627 804 1054 2937 4502
mlaII (GATC) :
 sau3AI (GATC) : 139 851 1095 1340 1646 1853 2254 2720 3697 3772 3783 3791 3869 3881 3986 4327
mlaII (GATC) :
 sau96I (GGNCC) : 4345 4391 4649 4666 4702
mlaII (GATC) :
 sau96I (GGNCC) : 641 1024 1445 [M.haeIII-] 1624 [dcm-] 2134 [M.haeIII-] 2476 [M.haeIII-]
mlaII (GATC) :
 sau96I (GGNCC) : 4065 [M.haeIII-] 4144 [M.haeIII-] 4161 4383 4999 [M.haeIII-]
mlaII (ACTACT) :
 scrFI (CCSGG) : 4501
mlaII (dcm-) (CCVGG) :
 scrFI (CCVGG) : 1443 1669 1997 2775 2810 3509 4205 4556
mlaII (GCATC) :
 sau3AI (GCATC) : 501 524 1627 3157 3278 3291
mlaII (TACGTA) :
 sau3AI (TACGTA) : 175 237 416 1252 1362 1606 1858 1867 1954 2032 2095 2806 2922 2977 2998 3218
mlaII (ACTAGT) :
 sau3AI (ACTAGT) : 4270 4480 4710
mlaII (AATATT) :
 sau3AI (AATATT) : 217
mlaII (AGGCT) :
 sau3AI (AGGCT) : 338
mlaII (CCMGG) :
 sau3AI (CCMGG) : 2275 4825
mlaII (TCCGA) :
 sau3AI (TCCGA) : 526 [dcm-]
mlaII (CGCCG) :
 sau3AI (CGCCG) : 637 [1554]
mlaII (GACNNNGTC) :
 sau3AI (GACNNNGTC) : 1453 2518 3230 4674
mlaII (GATC) :
 sau3AI (GATC) : 211 1203 1419 1429 1574 1600 1722 1819 2191 2292 2668 2688 2712 2730 2732 2835
mlaII (GATC) :
 sau3AI (GATC) : 3176 3757 4087 4580 4912
mlaII (GATC) :
 sau3AI (GATC) : 2874
mlaII (TCTAGA) :
 sau3AI (TCTAGA) : 368
mlaII (RGATCY) :
 sau3AI (RGATCY) : 850 1094 1339 1852 2253 2719 3771 3782 3868 3880 4648 4665
mlaII (CGGCCG) :
 sau3AI (CGGCCG) : 290 1199
mlaII (GAAANNNTTC) :
 sau3AI (GAAANNNTTC) : 2216 4618
 not found:

nflI (CTTAAAG), apal (GGGCC), asp718 (GGTACCC), asuII (TTCGAA), bglII (AGATCT), bspMI (ACCTGC), bssHII (GGCGC), bstBI (TTCCGA), bstEI (GGTNACC), bstXI (CCANNNNNNTGG), bsu36I (CCANNNNNNTGG), clai (ATCGAT), eco81I (CCTNAGG), econI (CCTNNNNNAGG), espI (GCTNAGC), kpnI (GGTACCC), mluI (ACGCCGT), mstII (CCATGG), ncoI (GGGCC), nruI (TCGGGA), paeR7I (CTCGAG), rsrII (CGGWCCG), sacI (GAGCTC), salI (CCGGG), smarI (GCCNNNNNGCC), sfII (GTCGAC), smarI (CCCGGG), xbaI (CTCGAG), xmaI (CCCGAG), xhoI (CTCGAG),

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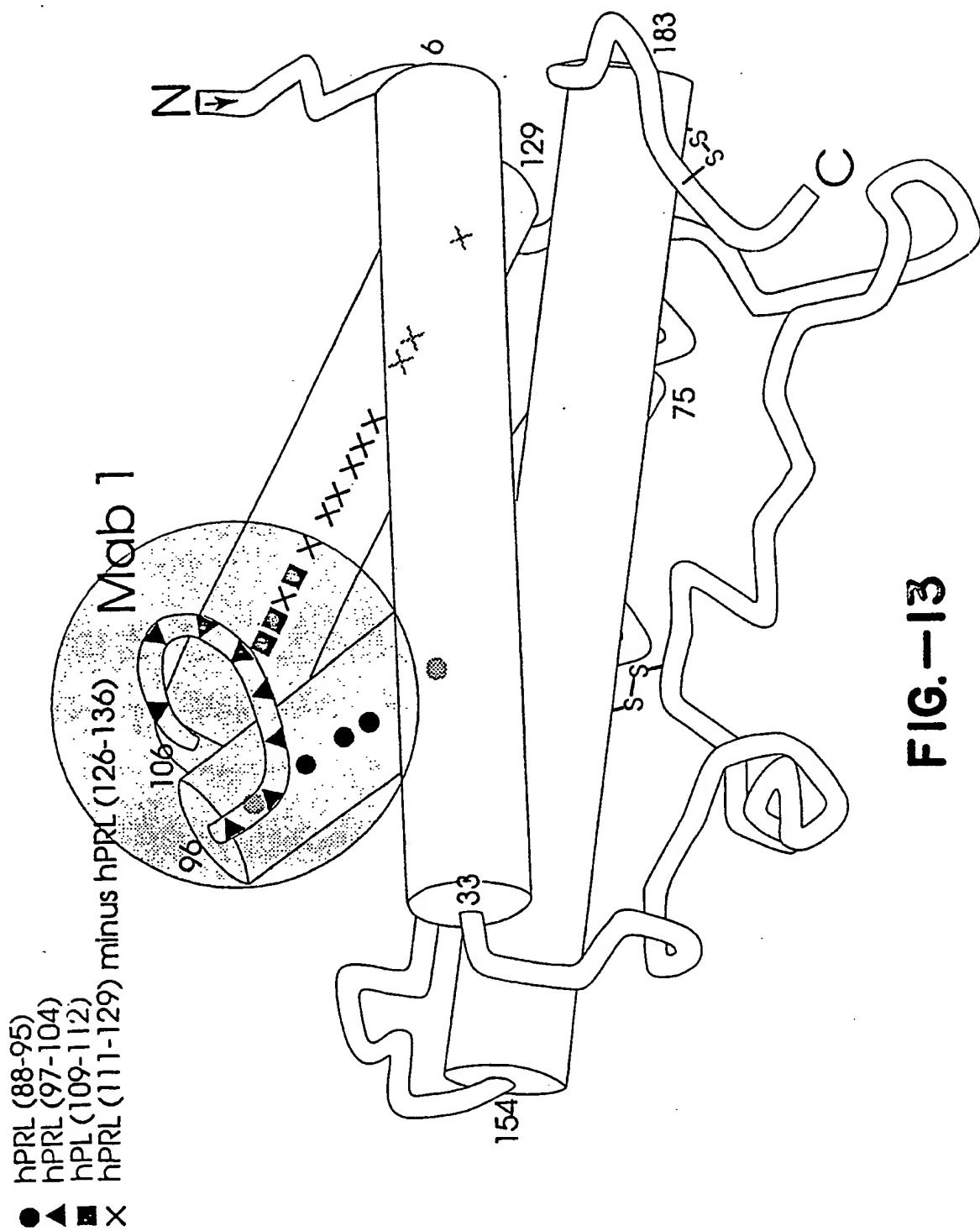


FIG. - 13

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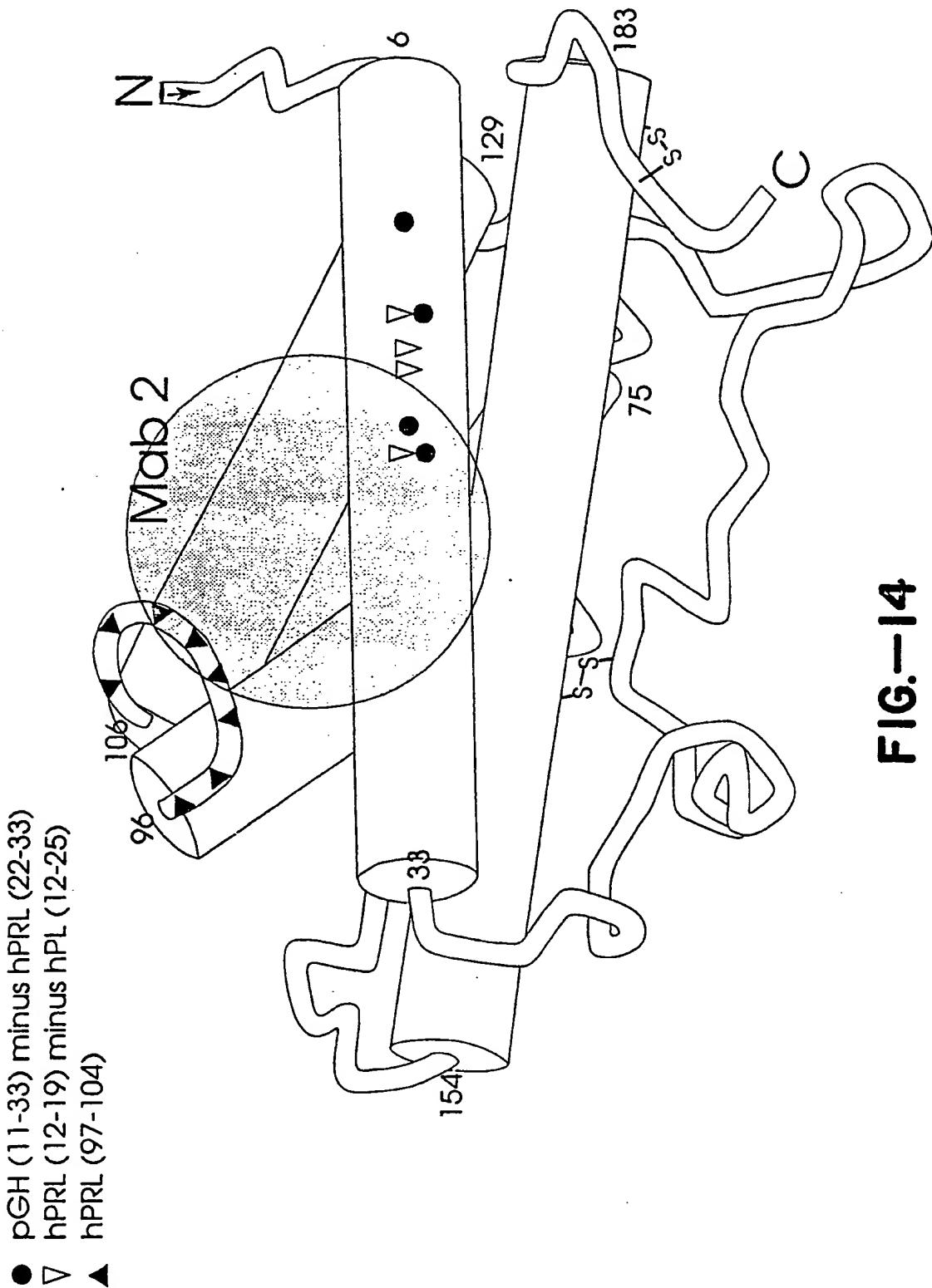


FIG.—14

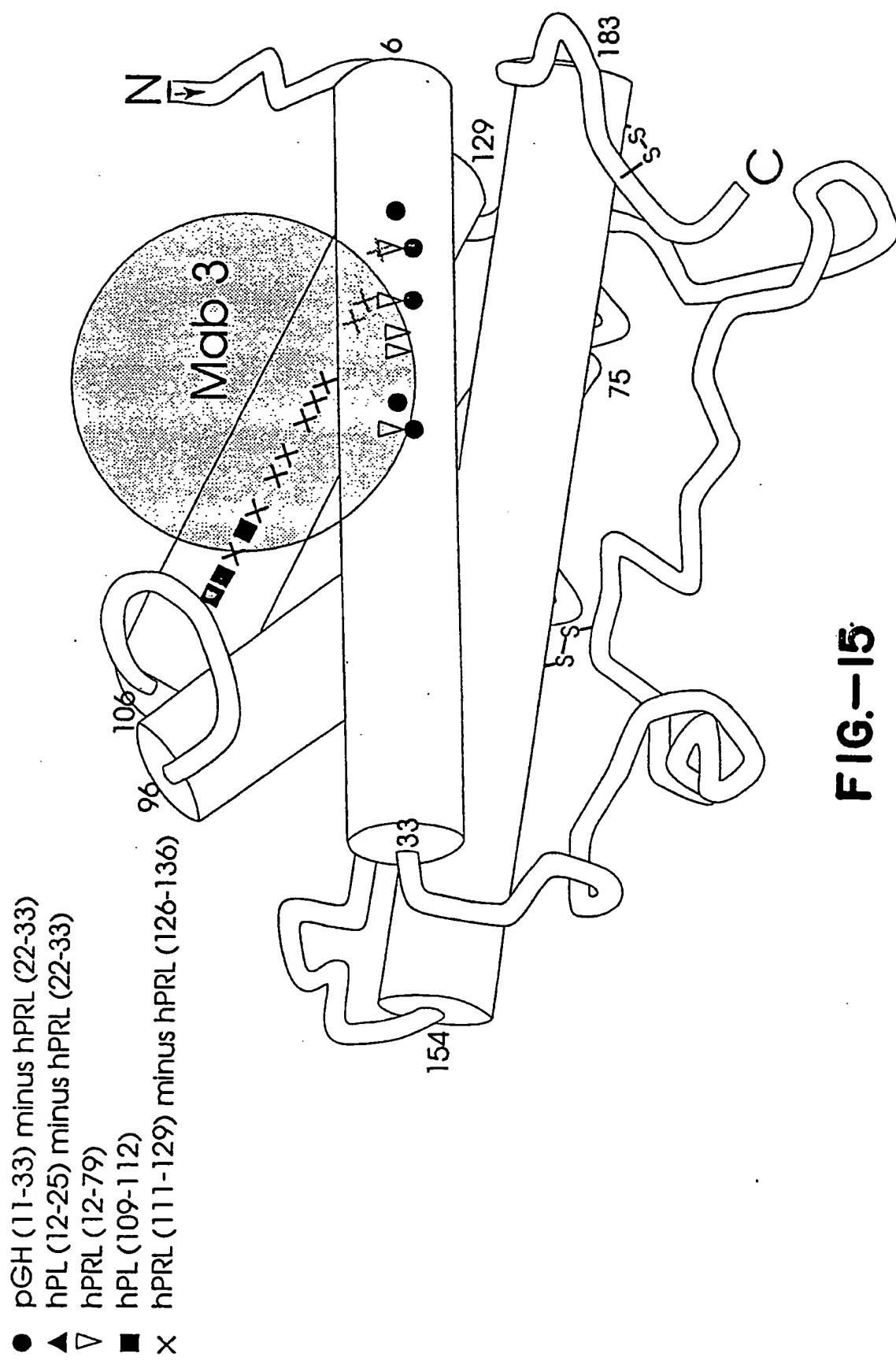


FIG.—15

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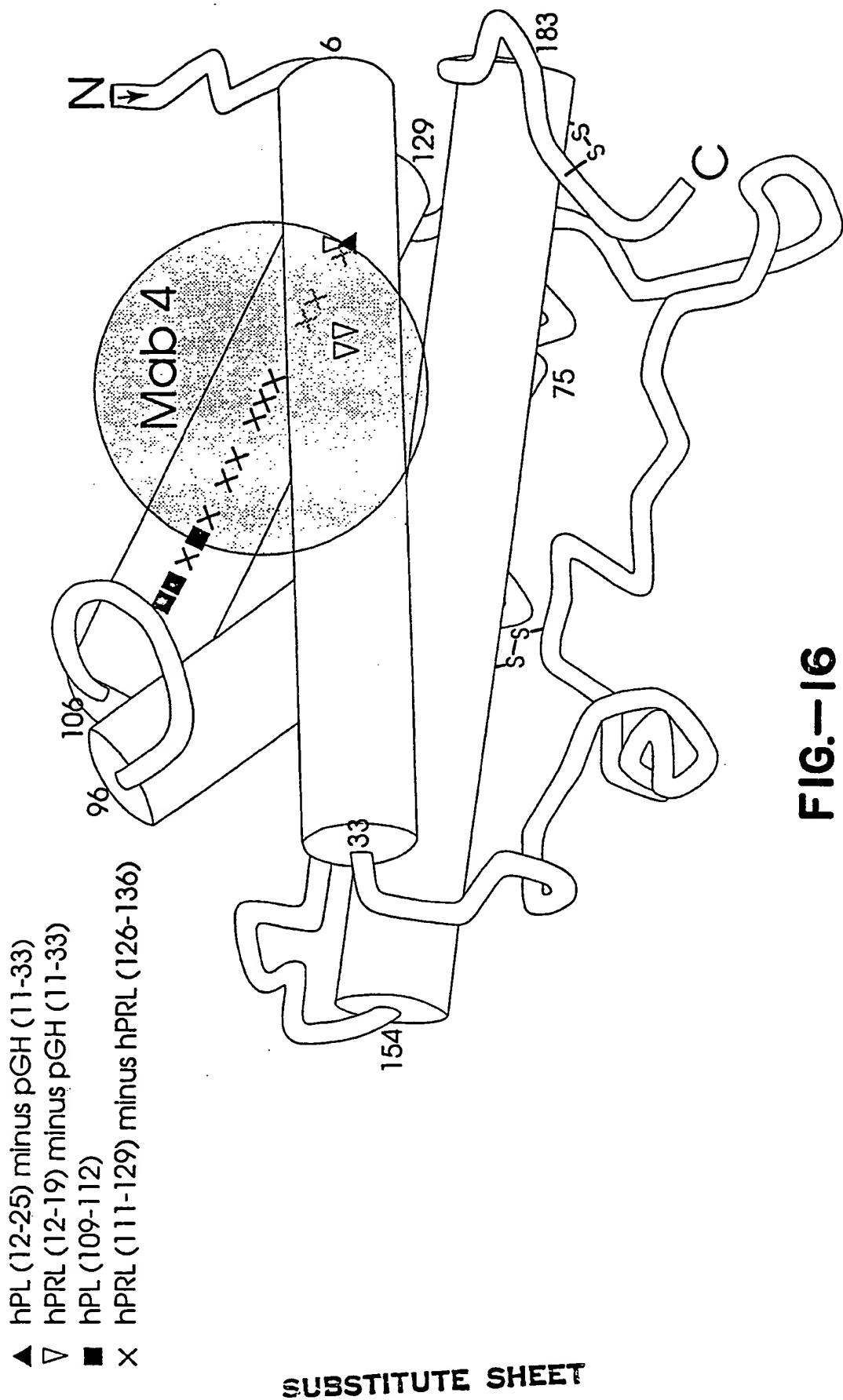


FIG.-16

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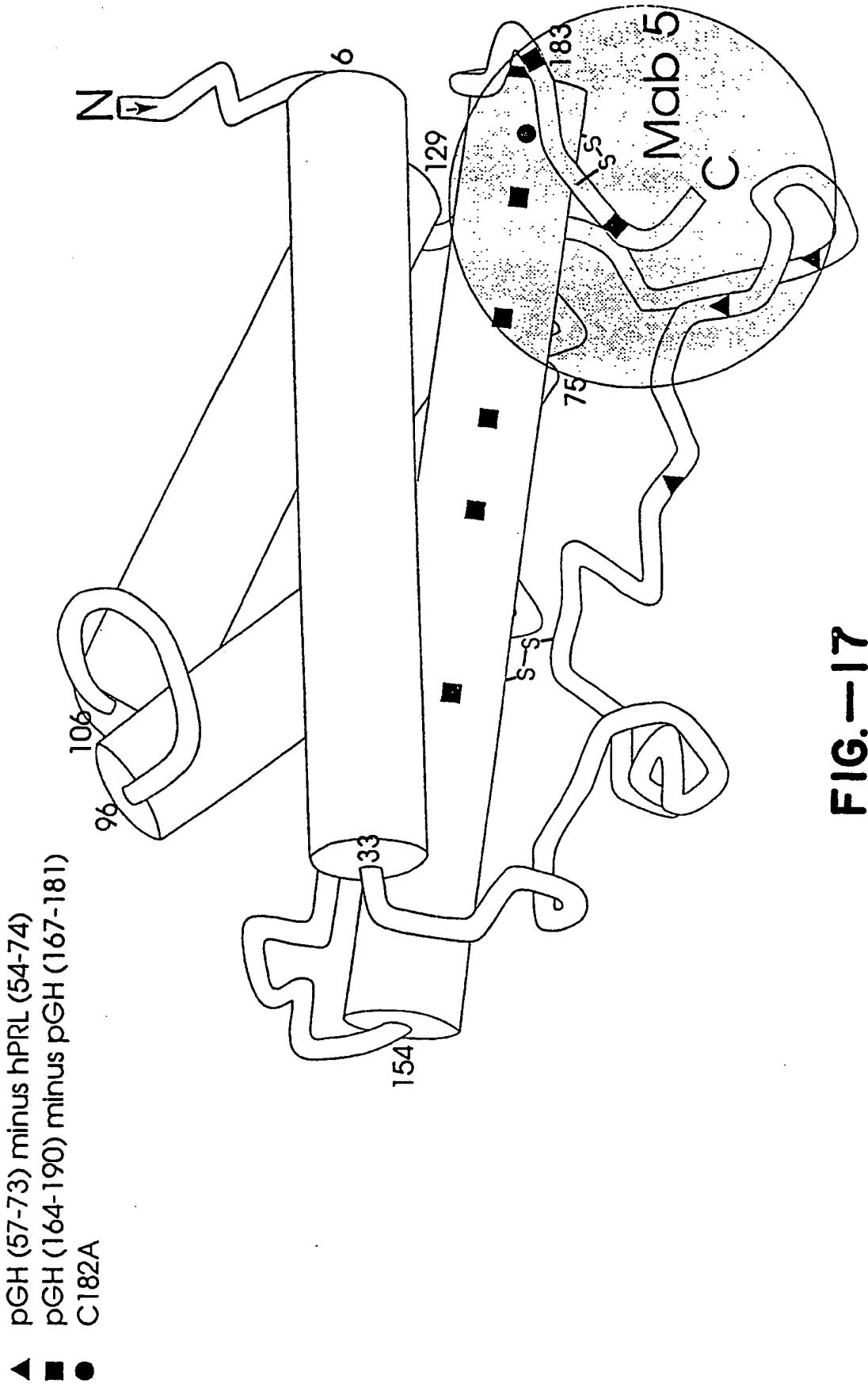


FIG. - 17

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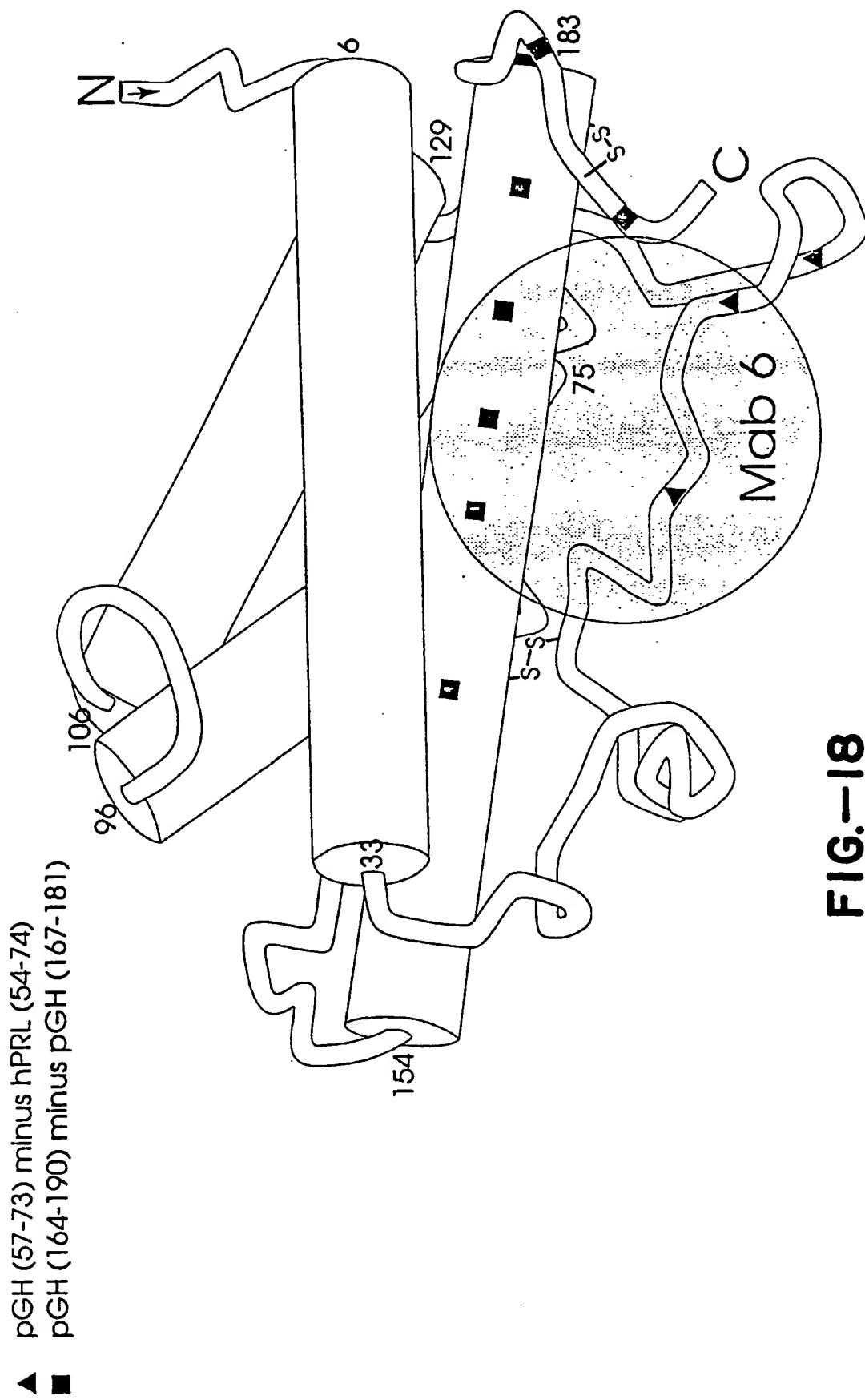


FIG.-18

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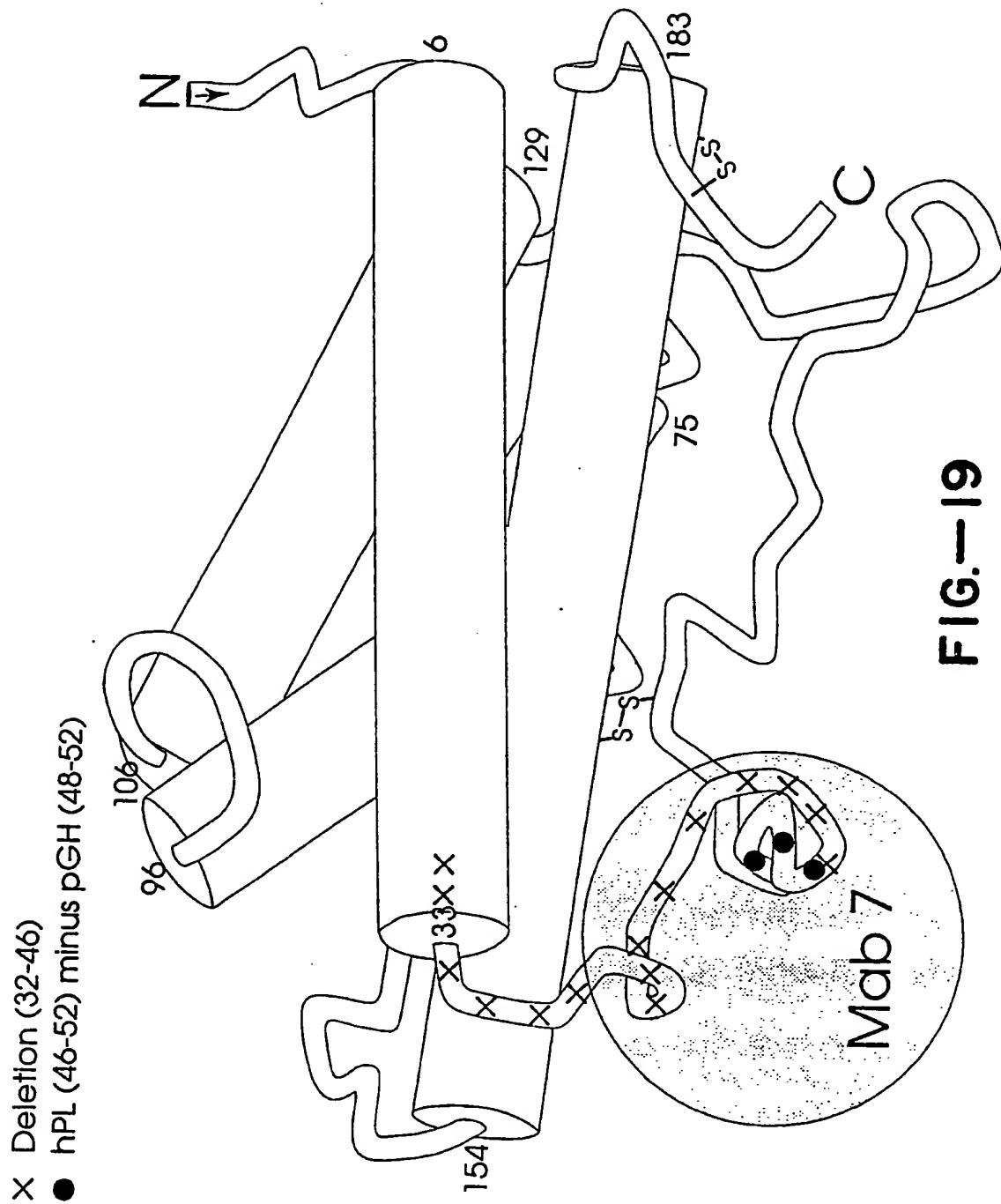


FIG.—19

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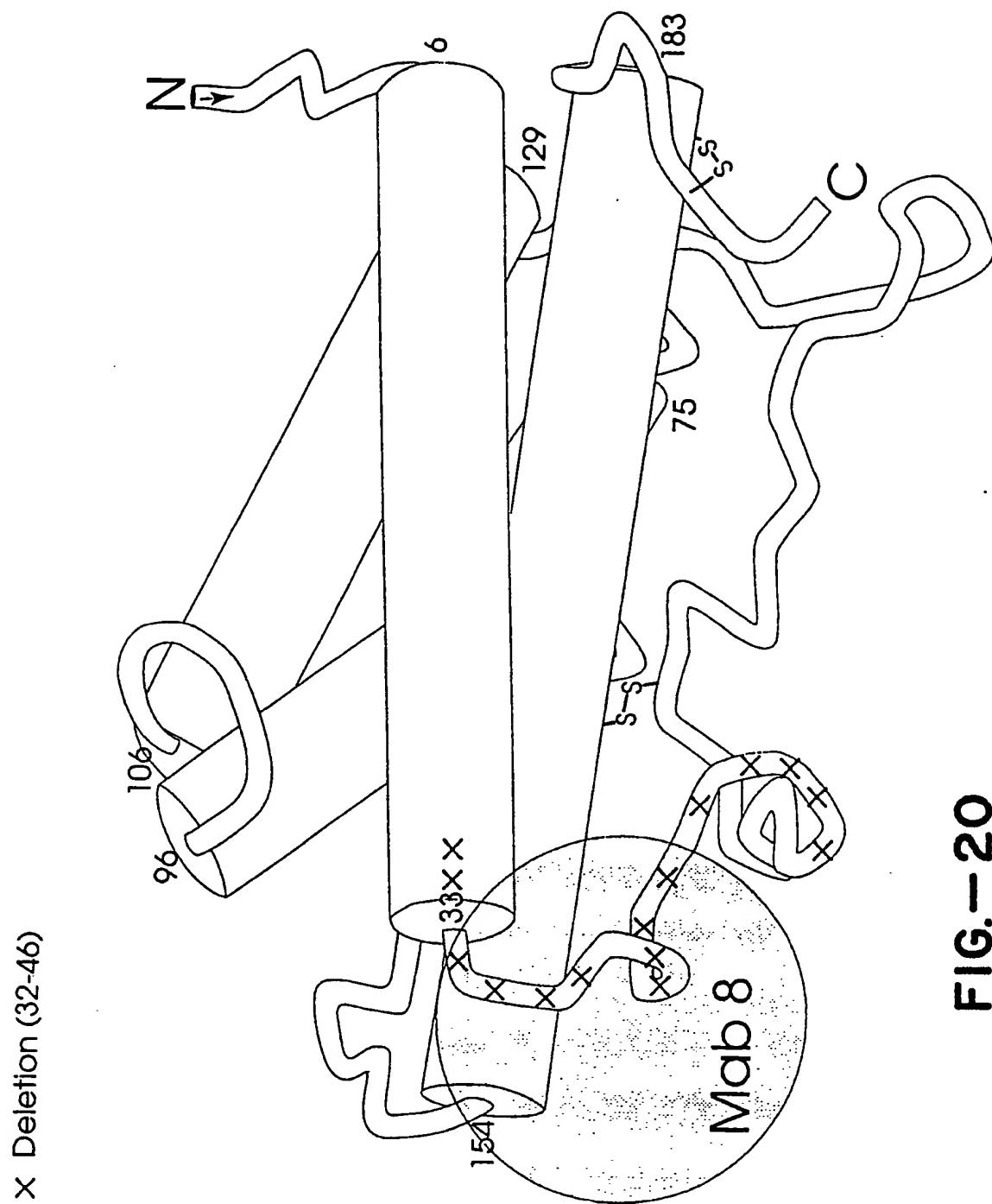


FIG.—20

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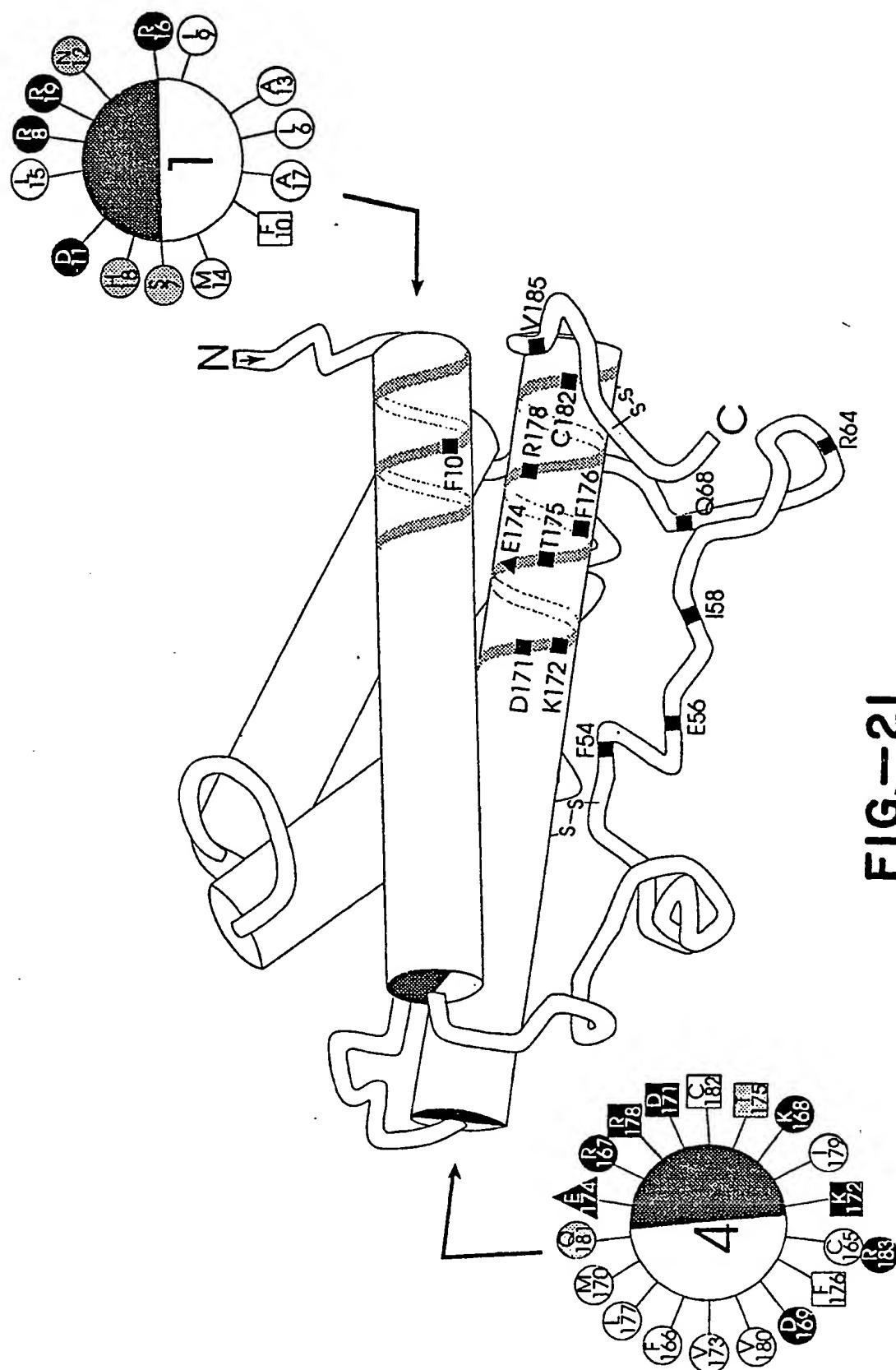


FIG.-21

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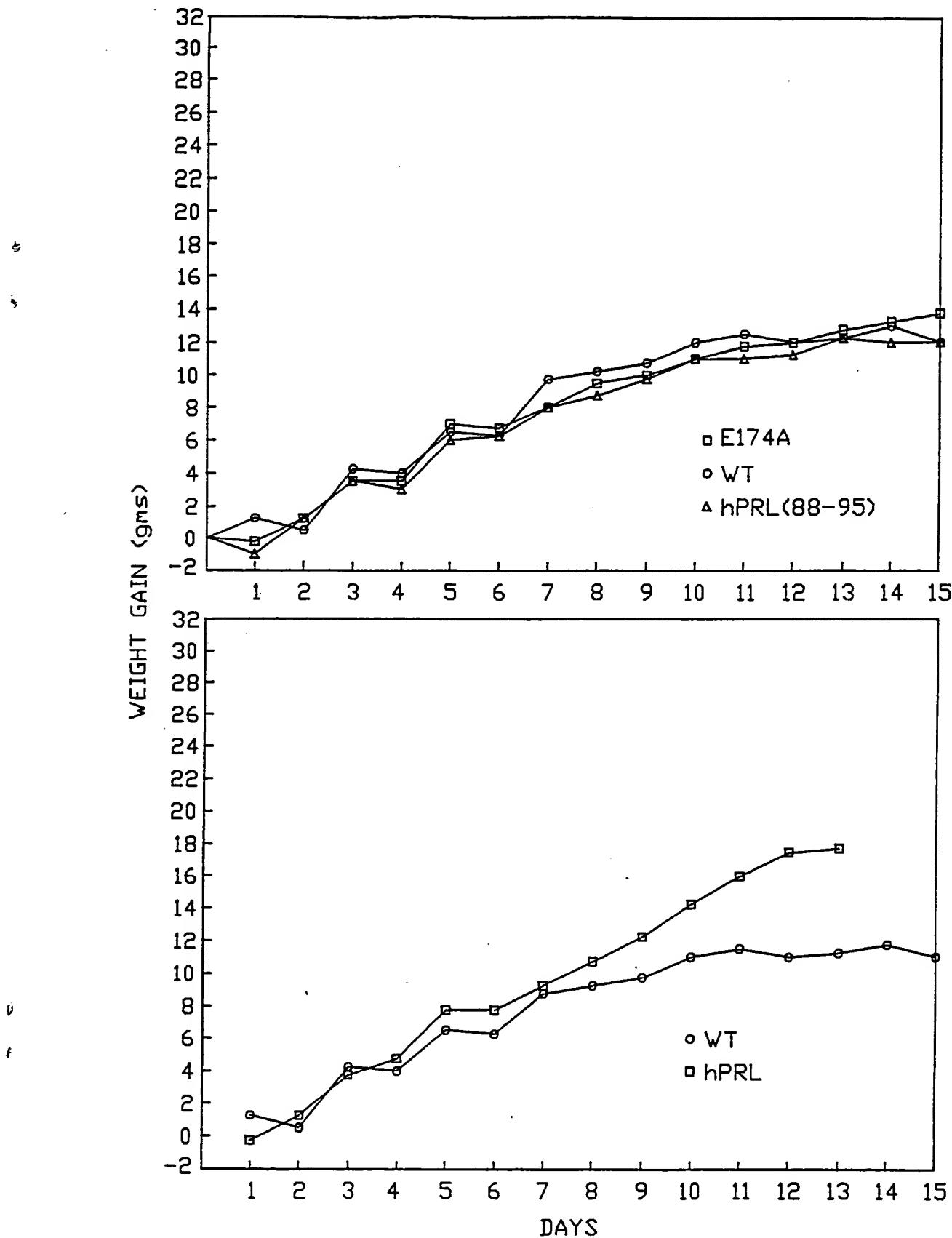


FIG.-22

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GH ANALOG BIOPOTENCY IN RATS AFTER 8 DAYS OF TREATMENT

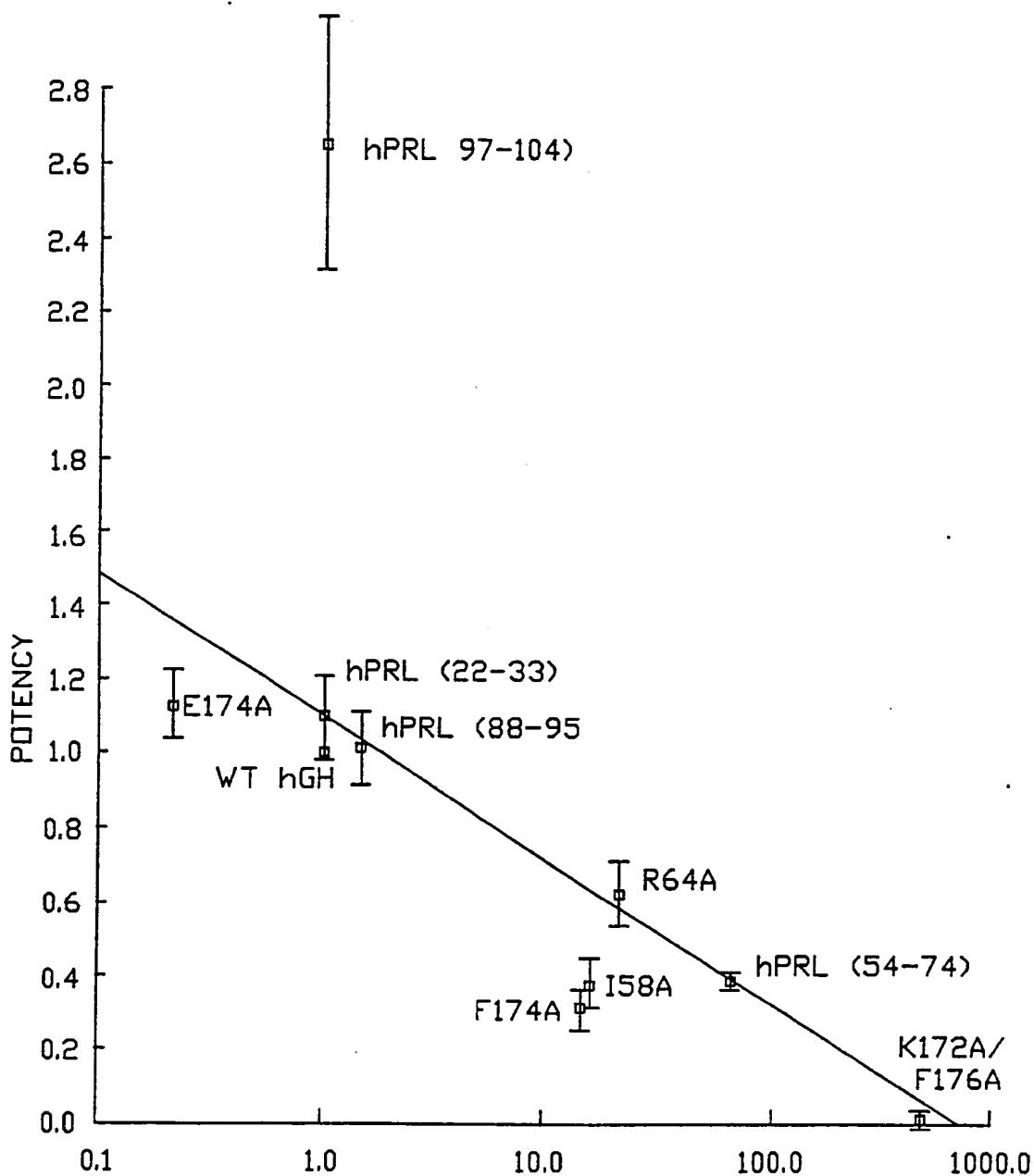


FIG.-23

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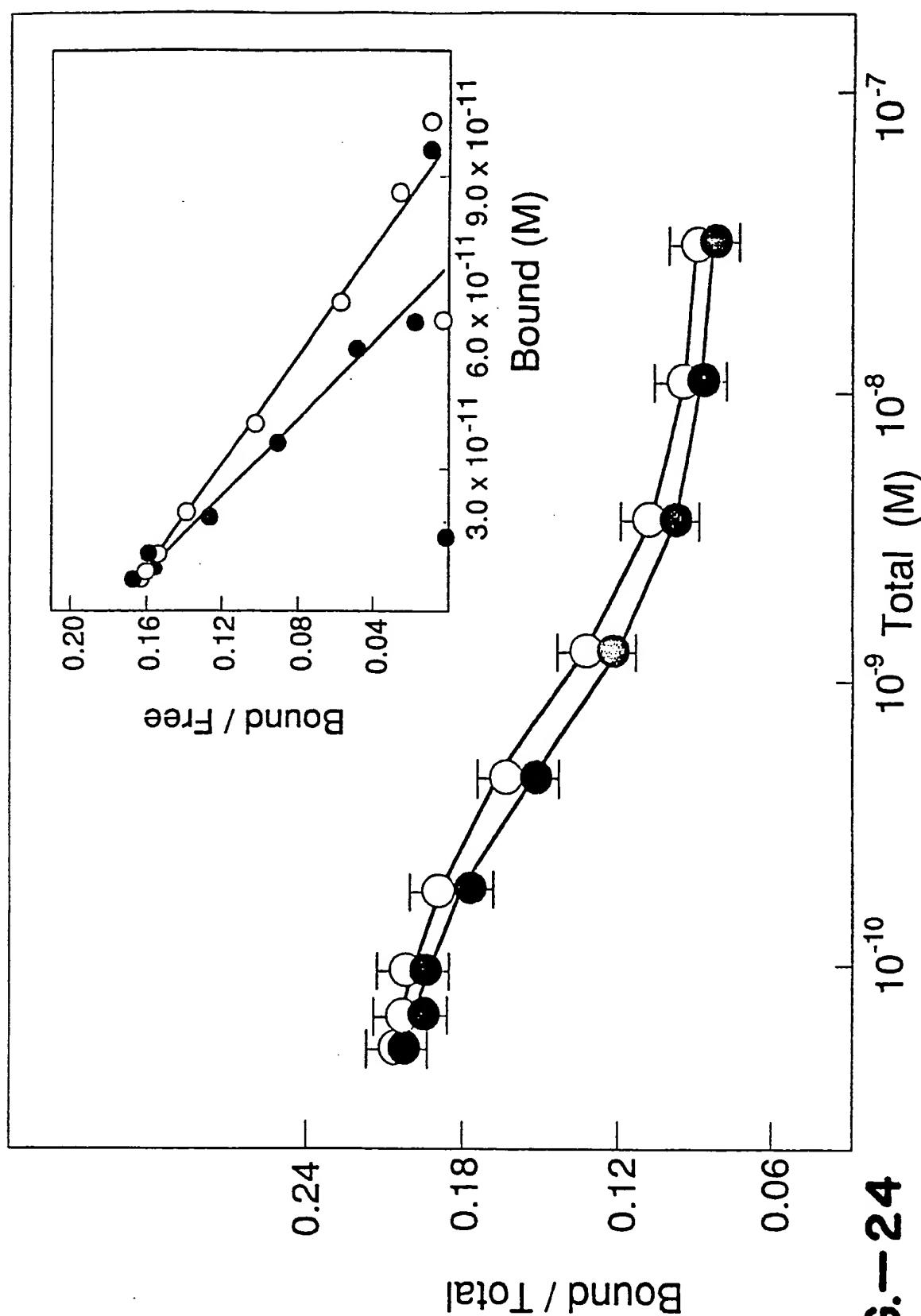


FIG.-24

Binding Determinants for hGHR

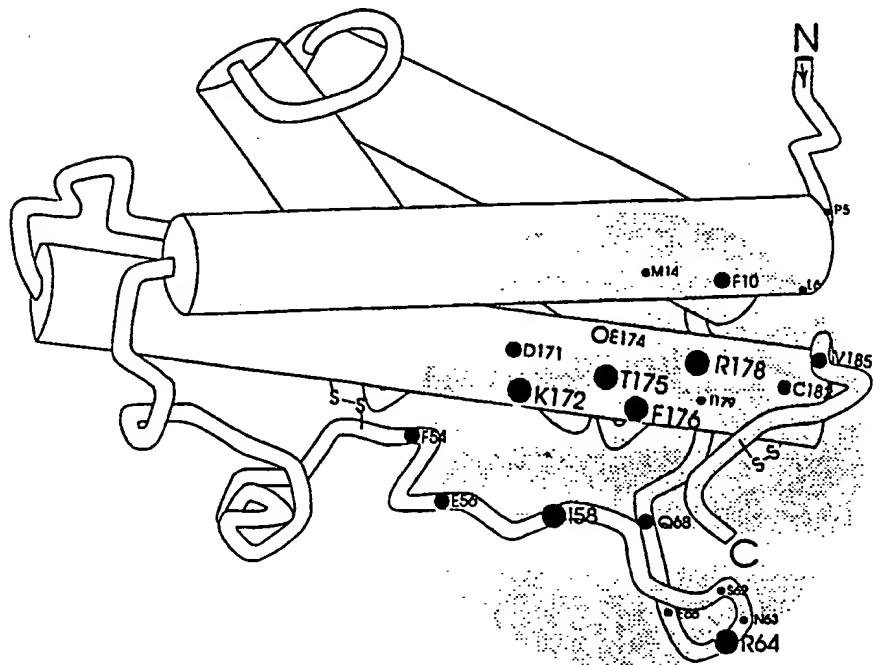


FIG.- 25A

Binding Determinants for hPRLr

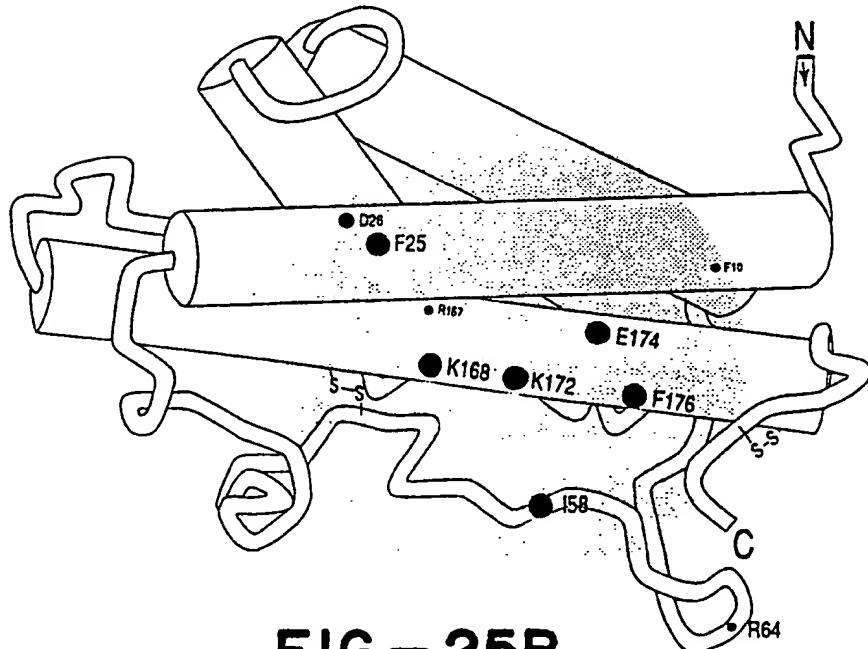


FIG.- 25B

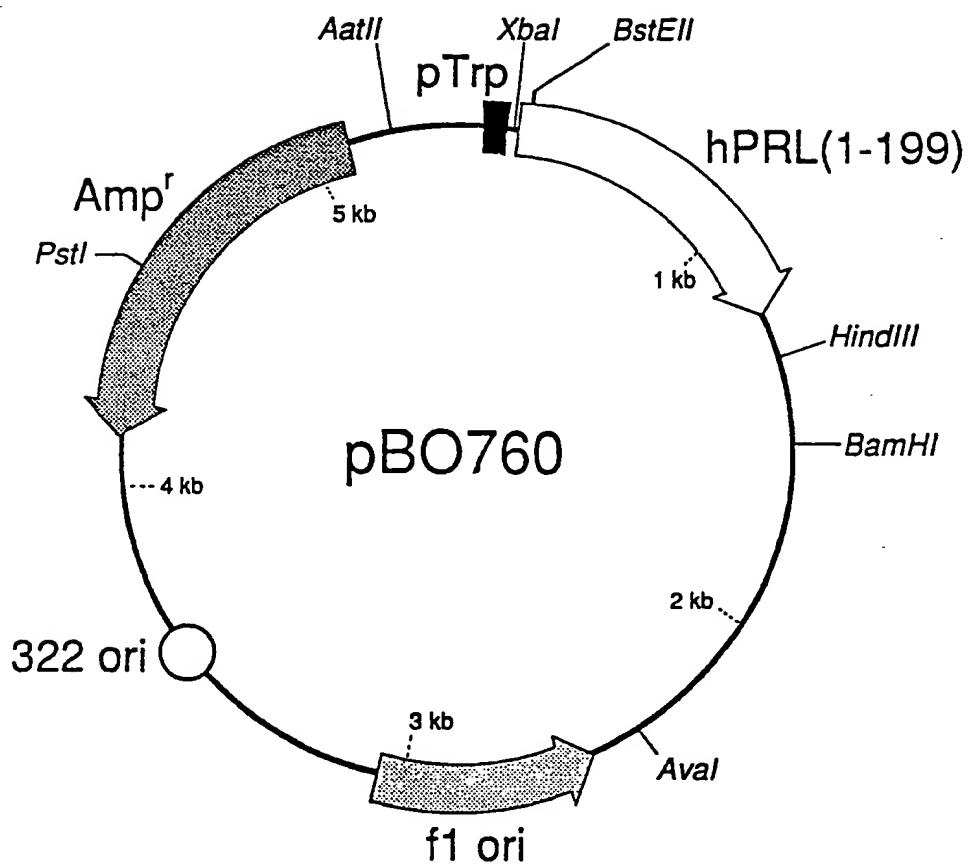


FIG.-26

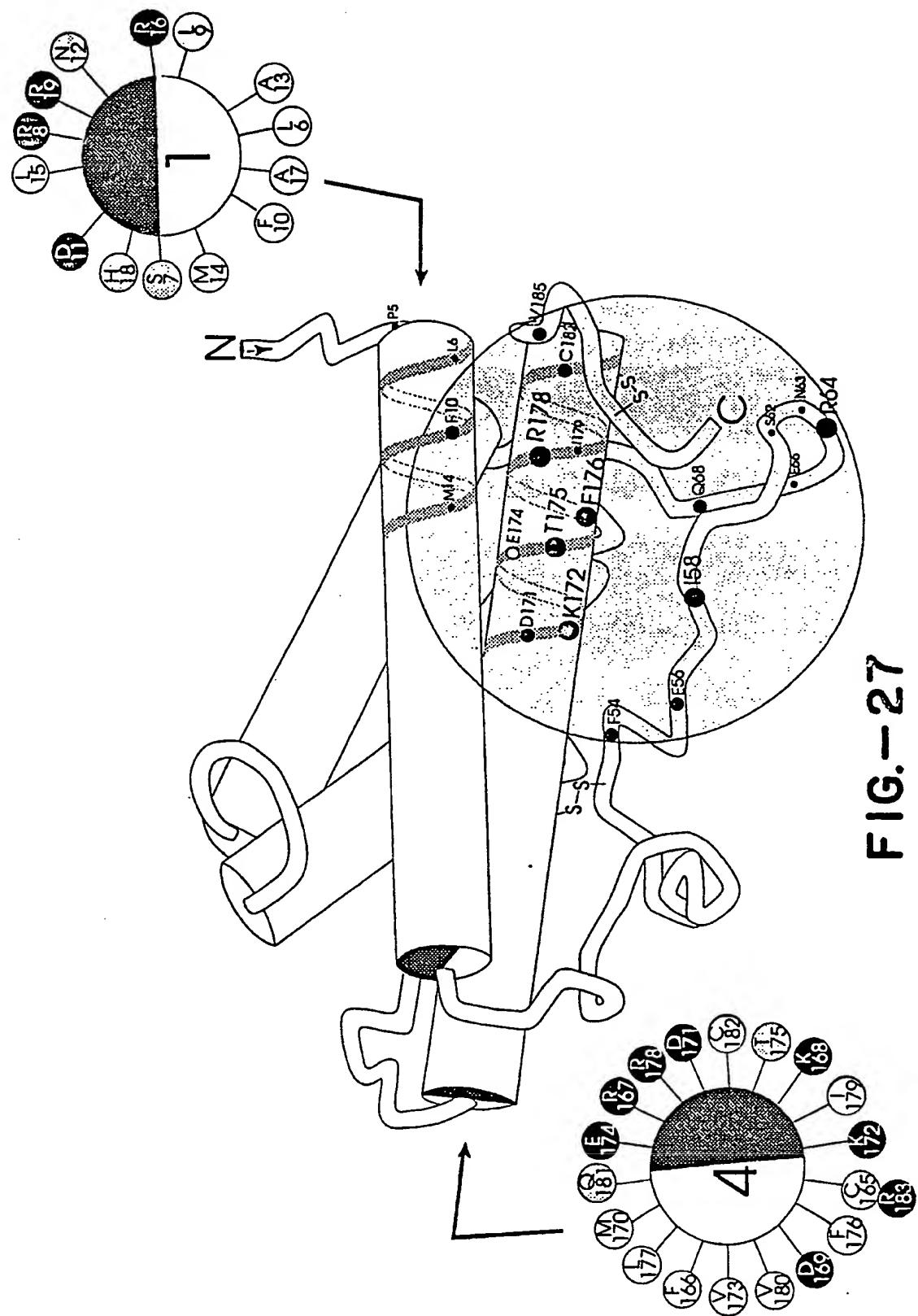


FIG.—27

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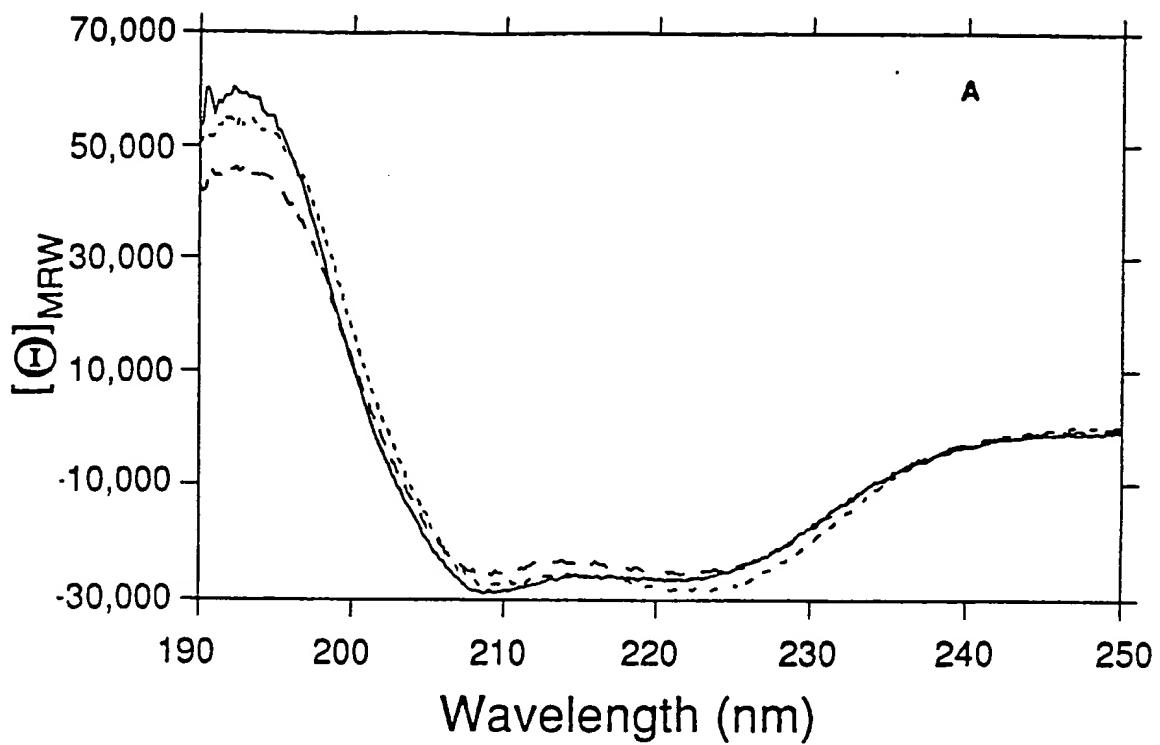


FIG.-28A

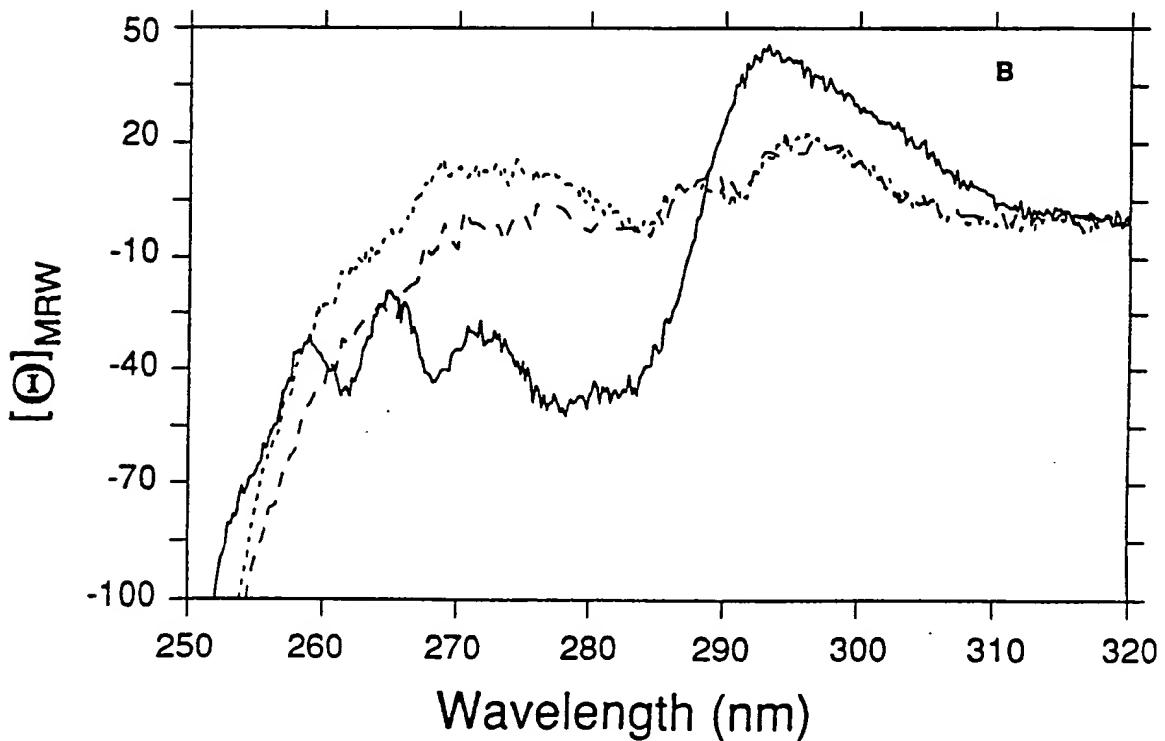


FIG.-28B

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FIG.-29

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INTERNATIONAL SEARCH REPORT

International Application No. PCT/US89/04778

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC (5): G01N 33/53, 31/00, 33/543, 33/567, 33/566

U.S. Cl: 435/7; 436/501, 504, 518, 548

II. FIELDS SEARCHED

Minimum Documentation Searched ⁷

Classification System	Classification Symbols
U.S.	435/7; 436/501, 504, 518, 548; 935/79, 81

Documentation Searched other than Minimum Documentation
to the Extent that such Documents are Included in the Fields Searched ⁸CHEMICAL ABSTRACTS SERVICE ONLINE, BIOSIS PREVIEWS,
AUTOMATED PATENT SYSTEMIII. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹

Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X,P	Science, Volume 244, issued 1989, CUNNINGHAM, B.C., ET AL, "High Resolution Epitope Mapping of hGH-Receptor Interactions by Alanine-Scanning Mutagenesis", 1081-1085.	1-13,16-31
X,P	Science, Volume 243, issued 1989, CUNNINGHAM, B.C., ET AL, "Receptor and Antibody Epitopes in Human Growth Hormone Identified by Homolog-Scanning Mutagenesis", 1330-1336.	1-13,16-31
A	Biochem. Biophys. Res. Commun., Volume 135, issued 1986, SOUROUTON, M.C., ET AL, "Localization of a Highly Immunogenic Region on the Acetylcholine Receptor Alpha-Subunit", 82-89.	1-13,16-31

* Special categories of cited documents: ¹⁰

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search

02 February 1990

Date of Mailing of this International Search Report

05 MAR 1990

International Searching Authority

ISA/US

Signature of Authorized Officer

Karen Krupen

KAREN I. KRUPEN

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	Endocrinol., Volume 121, issued 1987, WERTHER ET AL, "Localization and Characterization of Insulin Receptors in Rat Brain and Pituitary Gland Using In-Vitro Autoradiography and Computerized Densitometry, 1562-1570.	1-13,16-31
A	Endocrinology, Volume 107, issued 1980 MILLS, T.B. ET AL, "Fragments of human growth hormone produced by digestion with thrombin: chemistry and biological properties", 391-399 (See Abstract, 143544)	1-13,16-31
A	Chemical Abstracts, Volume 108, no. 11, issued 1988, (Columbus, Ohio, U.S.A) B. C. Cunningham, "Improvement in the alkaline stability of subtilisin using an efficient random mutagenesis and screening procedure", Abstract.	1-13,16-31

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE¹

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. Claim numbers , because they relate to subject matter¹² not required to be searched by this Authority, namely:

2. Claim numbers , because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out¹³, specifically:

3. Claim numbers , because they are dependent claims not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING²

This International Searching Authority found multiple inventions in this international application as follows:

(See Attachment).

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers: 1-13 and 16-31

4. As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

The additional search fees were accompanied by applicant's protest.

No protest accompanied the payment of additional search fees.

Part IV. Before #1, Observations

I. Claims 1-13 and 16-31 are drawn to a method for identifying unknown active domains in the amino acid sequence of polypeptides classified in class 436, subclass 501.

II. Claims 14, 15 and 32-64 are drawn to a method of forming a growth hormone variant and the growth hormone variants produced classified in class 530, subclass 350.

III. Claims 65-79 are drawn to human prolactin hormone variants classified in class 530, subclass 399.

IV. Claims 80-83 are drawn to human placental lactogen variants classified in class 530, subclass 399.

V. Claims 84-86 are drawn to DNA sequences and expression vectors and hosts classified in class 536, subclass 27.